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Pengaruh Intervensi BMF-219 Sebagai Inhibitor Menin Terhadap Proliferasi, Viabilitas dan Aktivitas Fosforilasi Oksidatif Lini Sel Kanker Pankreas PANC-1
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Universitas Gadjah Mada, 2026 | Diunduh dari http://etd.repository.ugm.ac.id/

INTISARI

Latar Belakang: *Pancreatic ductal adenocarcinoma* (PDAC) merupakan jenis kanker pankreas dengan prognosis yang buruk akibat sifat agresif dan resistensi terhadap terapi. Protein menin yang dikode oleh gen *MEN1* berperan dalam memperkuat aktivitas transkripsi MYC yang mendukung proliferasi, kelangsungan hidup, dan *reprogramming* metabolik sel kanker PDAC. BMF-219 (*icovamenib*) merupakan inhibitor menin kovalen yang berpotensi menghambat interaksi menin dan MYC.

Tujuan: Mengetahui pengaruh BMF-219 terhadap viabilitas, proliferasi, dan aktivitas fosforilasi oksidatif lini sel kanker pankreas PANC-1.

Metode: Penelitian eksperimental *in vitro* menggunakan lini sel PANC-1 dengan rancangan *post-test only control group*. Nilai IC_{50} ditentukan melalui kurva dosis-respons. Viabilitas sel diamati pada 24, 48, dan 72 jam menggunakan metode eksklusi *trypan blue*. Proliferasi dievaluasi melalui kurva pertumbuhan dan perhitungan *doubling time*. Aktivitas fosforilasi oksidatif dianalisis menggunakan Glycolysis/OXPHOS Assay Kit G270 berdasarkan pengukuran ATP total, ATP glikolitik, ATP mitokondria dan produksi laktat. Analisis statistik menggunakan *One-way* ANOVA dan *Two-way* ANOVA dengan uji lanjut Dunnett ($p<0,05$).

Hasil: BMF-219 memiliki nilai IC_{50} sebesar 2,137 µM pada 48 jam. Viabilitas sel PANC-1 pada kelompok yang diberi BMF-219 lebih rendah dibandingkan kelompok kontrol. Perlakuan BMF-219 juga menghambat proliferasi sel yang ditunjukkan oleh *doubling time* yang lebih tinggi dibandingkan kelompok kontrol. Analisis metabolisme menunjukkan bahwa sel PANC-1 dominan bergantung pada glikolisis. Setelah perlakuan BMF-219 selama 24 jam, kontribusi ATP mitokondria lebih rendah dibandingkan kontrol (2% vs 7%), sedangkan kontribusi ATP glikolitik lebih tinggi (98% vs 93%), menunjukkan penurunan aktivitas fosforilasi oksidatif.

Kesimpulan: BMF-219 menurunkan viabilitas dan proliferasi sel PANC-1 serta aktivitas fosforilasi oksidatif, sehingga mendukung potensi jalur menin–MYC sebagai target terapeutik pada PDAC.

Kata kunci: BMF-219, menin, MYC, PANC-1, fosforilasi oksidatif.

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ABSTRACT

Background: Pancreatic ductal adenocarcinoma (PDAC) is the most common type of pancreatic cancer and is associated with a poor prognosis due to its aggressive behavior and resistance to conventional therapies. Menin, encoded by the *MEN1* gene, enhances MYC transcriptional activity, thereby promoting cancer cell proliferation, survival, and metabolic reprogramming. BMF-219 (icovamenib) is a covalent menin inhibitor with the potential to disrupt the menin–MYC interaction.
Objective: To evaluate the effects of BMF-219 on cell viability, proliferation, and oxidative phosphorylation activity in the PANC-1 pancreatic cancer cell line.
Methods: An *in vitro* experimental study was conducted using PANC-1 cells with a post-test-only control group design. The IC_{50} value was determined from dose–response curve analysis. Cell viability was assessed at 24, 48, and 72 hours using the trypan blue exclusion method. Cell proliferation was evaluated through growth curve analysis and doubling time calculation. Oxidative phosphorylation activity was analyzed using the Glycolysis/OXPHOS Assay Kit G270 by measuring total ATP, glycolytic ATP, mitochondrial ATP, and lactate production. Statistical analyses were performed using one-way and two-way ANOVA followed by Dunnett's post hoc test, with $p<0.05$ considered statistically significant.
Results: BMF-219 exhibited an IC_{50} value of 2.137 µM at 48 hours. Cell viability in BMF-219-treated groups was lower than that of the control group. BMF-219 also inhibited cell proliferation, as indicated by a longer doubling time compared with the control group. Metabolic analysis revealed that PANC-1 cells predominantly relied on glycolysis. Following 24 hours of treatment, the contribution of mitochondrial ATP was lower than in the control group (2% vs. 7%), whereas the contribution of glycolytic ATP was higher (98% vs. 93%), suggesting a reduced oxidative phosphorylation activity.
Conclusion: BMF-219 reduced PANC-1 cell viability and proliferation and showed a tendency to decrease oxidative phosphorylation activity, supporting the therapeutic potential of targeting the menin–MYC pathway in PDAC.
Keywords: BMF-219, menin, MYC, PANC-1, oxidative phosphorylation.