Kombinasi Penghambat Poli-ADP Ribosa Polimerase (PARP) dan Antiandrogen Dibandingkan dengan Antiandrogen dalam Pengelolaan Kanker Prostat Metastasis Resisten Kastrasi: Tinjauan Sistematis dan Meta-Analisis = Combination of Poly-ADP Ribose Polymerase (PARP) Inhibitor and Antiandrogen as Compared to Antiandrogen in The Management of Metastatic Castration-Resistant Prostate Cancer: Systematic Review & Meta Analysis

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Abstrak

Pendahuluan: Kanker prostat merupakan jenis kanker yang paling sering kedua dan penyebab kematian kelima terbanyak di kalangan pria di seluruh dunia. Meskipun ada kemajuan dalam terapi, masalah kekambuhan dan resistensi terhadap pengobatan masih menjadi perhatian, seperti kanker prostat metastasis resisten kastrasi (MCRPC) yang tidak merespons terapi pengurangan androgen tradisional. Penghambat Poly ADP-ribose polymerase (PARP) dianggap sebagai pengobatan yang menjanjikan untuk pasien MCRPC. Oleh karena itu, kombinasi terapi PARP dan antiandrogen perlu dievaluasi.
Bahan & Metode: Review sistematis dilakukan dengan mengikuti panduan Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA). Pencarian literatur dilakukan pada lima basis data yang berbeda dan disaring sesuai dengan kriteria PICO yang ditentukan. Pengambilan data dilakukan untuk membandingkan Kelangsungan Hidup Bebas Progresi (PFS), Kelangsungan Hidup Keseluruhan (OS), Kualitas Hidup Terkait Kesehatan (HRQOL), dan efek samping, dilanjutkan dengan analisis kuantitatif.
Hasil & Diskusi: Sebanyak empat RCT yang memenuhi syarat, termasuk dua studi besar, dimasukkan dalam penelitian ini. Analisis PFS menunjukkan penurunan risiko yang signifikan dengan rasio bahaya (HR) sebesar 0.53 (95% CI 0.43-0.66;p<0.001). Hasil serupa juga ditemukan dengan penurunan risiko kematian dengan OS HR sebesar 0.75 (95% CI 0.58-0.97;p=0.03). Analisis HRQOL pada Functional Assessment of Cancer Therapy - Prostate (FACT-P) melaporkan hasil yang tidak signifikan [HR=0.97 (95% CI 0.80-1.17;p=0.72)], dengan hasil serupa pada skor rasa sakit terburuk BPI-SF [HR=0.66 (95% CI 0.32-1.35;p=0.26). Analisis efek samping cukup menarik dengan penurunan risiko pada efek samping ringan dan risiko lebih besar pada kejadian efek samping yang parah, dengan efek kumulatif perbedaan efek samping yang tidak signifikan antara kedua kelompok [HR=1.13 (95% CI 0.79-1.62;p=0.49).
Kesimpulan: Penambahan penghambat PAPR pada pengobatan pasien mCRPC secara signifikan meningkatkan PFS dan OS tanpa memberikan dampak negatif pada HRQoL dan efek samping. Studi lanjutan harus dilakukan untuk menentukan manfaatnya dalam berbagai pengaturan.
.....ntroduction: Prostate cancer is the second most common cancer and the fifth leading cause of death among men worldwide. Despite the advancement in therapy, recurrence and resistancy after treatment is still a concerning issue, such as metastatic castration-resistant prostate cancer (MCRPC) which is resistant to traditional androgen-deprivation therapy (ADT). Poly ADP-ribose polymerase (PARP) inhibitor is hailed as a promising treatment for MCRPC patients. Thus, combination therapy on PARP and antiandrogen should be evaluated.
Material & Methods: Systematic review was conducted by adhering to the Preferred Reporting Items for

Systematic Review and Meta-Analysis (PRISMA) statement. The literature search were conducted on five different databases and screened against the predetermined PICO criteria. Data extraction were completed to compare Progression-Free Survival (PFS), Overall Survival (OS), Health-Related Quality of Life (HRQOL), and adverse effects, continued by quantitative analysis
Results & Discussion: A total of four eligible RCTs, comprising of two large studies were included. The PFS analysis has reported significant risk reduction with hazard ratio (HR) of 0.53 (95% CI 0.43-0.66;p<0.001). Similar results are also found with reduced risk of death with OS HR of 0.75 (95% CI 0.58-0.97;p=0.03). The HRQOL analysis on Functional Assessment of Cancer Therapy - Prostate (FACT-P) reported insignificant results [HR=0.97 (95% CI 0.80-1.17;p=0.72)], with similar results with the BPI-SF worst pain score [HR=0.66 (95% CI 0.32-1.35;p=0.26). The adverse effects analysis was quite interesting with risk reduction on mild adverse effects and
greater risk in severe adverse events, with a cumulative effect of insignificant adverse events difference among the two group [HR=1.13 (95% CI 0.79-1.62;p=0.49).
Conclusion: The addition of PAPR inhibitor to the treatment of mCRPC patients has significantly improved the rPFS and OS with no negative impact on HRQoL and adverse effects. Further studies should be conducted to determine the benefits in various settings.