

INTISARI

Asam zoledronat dan asam ibandronat merupakan terapi metastase tulang pada multiple mieloma (MM). Asam zoledronat lebih efektif mencegah *skeletal related event* (SRE) namun *adverse event* (AE) pada fungsi ginjal dan *osteonecrosis* rahang (ONJ) lebih banyak terjadi. Tujuan penelitian ini adalah menganalisis besarnya biaya terapi metastase tulang pada MM dengan asam zoledronat dan asam ibandronat, menganalisis besarnya nilai *incremental cost effectiveness ratio* (ICER) per efektivitas dalam mencegah SRE dan menganalisis apakah asam zoledronat lebih *cost* efektif terhadap asam ibandronat berdasarkan nilai ICER per *quality adjusted life years* (QALY) pada pasien MM.

Penelitian farmakoeкономи ini dilakukan melalui analisa *cost of illness* (COI), *cost effectiveness analysis* (CEA) dan *cost utility analysis* (CUA). Rancangan penelitian *cross sectional* digunakan pada penelitian COI. Biaya dihitung dari perspektif *provider* (biaya medis langsung) dan *societal* (biaya non medis langsung dan biaya tidak langsung). *Cohort* retrospektif digunakan pada penelitian CEA dengan *outcome* klinik berupa *time to SRE* dan persentase AE. ICER per efektivitas dihitung sebagai biaya per 1 tahun *time to SRE*. CUA menggunakan pendekatan *modelling*, *utility* sebagai parameter model diteliti dengan rancangan *cross sectional*. Markov model dengan 3 *state* yaitu *No SRE*, *SRE* dan *death*, siklus 4 minggu dan *time horizon life time*. Model disimulasikan pada perspektif *provider* dan *societal*. ICER dianalisa sebagai *cost* per QALY kemudian dibandingkan dengan *cost effectiveness threshold* (Rp. 177.300.000). Analisa sensitivitas satu arah, sensitivitas probabilistik dan CEA *curve* (CEAC) dilakukan untuk menguji ketahanan model.

Biaya medis obat asam zoledronat setiap siklus lebih murah dari asam ibandronat (Rp. 1.765.430 *versus* Rp. 2.513.438). Biaya non medis langsung dan biaya tidak langsung pada kondisi *SRE* lebih besar dari pada kondisi *No SRE*. *Time to SRE* asam zoledronat adalah 2,12 bulan lebih lama dari asam ibandronat. Hasil observasi AE pada asam zoledronat dan asam ibandronat pada gangguan ginjal adalah 2,5% (1/40) *versus* 3,3% (1/30) dan gejala mirip flu adalah 2,5% (1/40) *versus* 6,7% (2/30). Asam zoledronat memberikan tambahan QALY sebesar 0,95 tahun dibandingkan asam ibandronat. Nilai ICER per QALY asam zoledronat terhadap asam ibandronat pada asumsi tanpa kemoterapi dengan perspektif *provider* adalah – Rp. 17.394.174, perspektif *societal* adalah - Rp. 66.779.334. Penambahan biaya kemoterapi menghasilkan nilai ICER per QALY sebesar –Rp. 17.296.207 sampai dengan -Rp.17.286.507 pada perspektif *provider* serta – Rp. 69.074.942 sampai dengan – Rp. 68.980.953 perspektif *societal*. Biaya pada terapi asam zoledronat Rp. 87.694.119 ± Rp. 57.224.493 sedangkan pada terapi asam ibandronat adalah Rp. 106.856.703 ± Rp. 85.302.322). Nilai ICER adalah – Rp. 108.467.458 per 1 tahun *time to SRE*. Asam zoledronat *cost* efektif (*cost saving*) terhadap asam ibandronat dalam mencegah *SRE*. Implikasi hasil penelitian adalah asam zoledronat merupakan rekomendasi untuk terapi metastase tulang terbaik bagi MM sehingga perlu dilakukan analisa farmakoekonomi lebih lanjut bagi obat-obatan pencegah SRE lain untuk dimasukkan ke dalam formularium nasional.

Kata kunci : asam zoledronat, asam ibandronat, metastase tulang, multiple mieloma, farmakoekonomi

ABSTRACT

Zoledronic acid and ibandronic acid are therapy of bone metastases in multiple myeloma (MM). Zoledronic acid is more effective for the prevention of skeletal-related events (SRE) but the adverse events (AE) of kidney function and osteonecrosis of the jaw (ONJ) is more common. The study aimed to analyze the value of cost therapy of bone metastasis with zoledronic acid and ibandronic acid in MM, to analyze the value of *incremental cost effectiveness ratio* (ICER) per effectivity of SRE prevention and to analyze whether zoledronic acid was more cost effective compared to ibandronic acid from ICER per *quality adjusted life years* (QALY) in MM patients.

The pharmacoeconomic study was done through analysis of *cost of illness* (COI), *cost effectiveness analysis* (CEA) dan *cost utility analysis* (CUA). The cross sectional research design was used in COI research. costs were calculated from the provider's perspective (direct medical cost) and societal (direct non-medical costs and indirect costs). The cohort retrospective design was used in CEA research, the clinical outcomes were time to SRE and AE percentage. The ICER per effectiveness of SRE prevention was calculated as cost per one year time to SRE. Modelling approach was used in CUA research, utility as model parameter was studied with a cross-sectional design. Markov model with three states, namely No SRE, SRE, and death with a four-week cycle and time horizon life time. The model was simulated from a provider and societal perspective. ICER was analyzed as cost per quality-adjusted life years (QALY) gained. ICER per QALY gained compared to the cost-effectiveness threshold (Rp. 177,300,000). One-way sensitivity analysis, probabilistic sensitivity analysis, and CEA curve (CEAC) were performed to test the model's robustness.

The medical cost of zoledronic acid per cycle was less than ibandronic acid (IDR 1,765,430 versus IDR 2,513,438). The direct non-medical costs and indirect costs in the SRE condition are greater than the No SRE conditions. The time to SRE of zoledronic acid was 2.12 months longer than ibandronic acid. The results of AE's observations on zoledronic acid and ibandronic acid in kidney disorders were 2.5% (1/40) versus 3.3% (1/30) and flu like symptoms were 2.5% (1/40) versus 6.7% (2/30). Zoledronic acid provided an additional QALY of 0.95 years compared to ibandronic acid. The ICER value per QALY of zoledronic acid against ibandronic acid on the assumption without chemotherapy from the provider perspective was - IDR 17,394,174, the societal perspective was - IDR 66,779,334. The addition of chemotherapy costs resulted ICER value per QALY of -IDR 17,296,207 to -IDR 17,286,507 from the provider's perspective and - IDR 69,074,942 to - IDR 68,980,953 societal perspective. The costs of zoledronic acid therapy was IDR 87,694,119 ± IDR 57,224,493 and cost of ibandronic acid therapy was IDR 106,856,703 ± IDR 85,302,322. ICER per effectiveness was - IDR 108,467,458 per 1 year time to SRE. Zoledronic acid was cost-effective (cost saving) against ibandronic acid. The implication of the results was that zoledronic acid was the best recommendation for bone metastase therapy so the further pharmacoeconomics analysis need to be done to other SRE preventive drugs to be included in the national formulary.

Keywords: zoledronic acid, ibandronic acid, bone metastases, multiple myeloma, pharmacoeconomic