Diagnosing and Classifying Acute Leukemia Patients Through Immunophenotyping by Flow Cytometry in Indonesia

Dody Ranuhardy[a], Resti Mulyasari[a], Agus Susanto Kosasih[a], Lyana Setiawan[a], Yan Ma[b], Caitlin Asjes[b], Kristin Hui Xian Tan[b]

[a]Rumah Sakit Kanker Dharmais, Jakarta, Indonesia
[b]Becton Dickinson Holdings Pte Ltd, Singapore, Singapore

Introduction

In 2018, there were 13,500 new cases and 11,300 deaths from leukemia in Indonesia[1]. Leukemia alone costed Indonesia over IDR328 billion (USD20 million)[2]. Effective treatment for acute leukemia is only possible with accurate disease lineage classification (i.e. acute myeloid leukemia, acute lymphocytic leukemia). This study aims to compare the clinical and economic value of diagnosing patients by current local diagnostics standard (morphology and cytochemical test) versus proposed diagnostics (flow cytometry) for acute leukemia classification in Indonesia class A hospitals.

Methods

A decision tree reflecting current referral pathway based on morphology and cytochemical test (**Figure 1**) and another for proposed referral pathway using flow cytometry (**Figure 2**) were developed in Microsoft Excel. Budget impact analysis was conducted comparing cost outcomes of the two decision trees. Other outcomes estimated and compared include patients accurately diagnosed, average time to diagnosis and average prognosis. Due to the lack of publicly available data, local oncology and pathology experts were interviewed for the parameters presented in **Table 1**.

Table 1: Estimates obtained through interviews with local oncology and pathology experts

Parameters	Estimates
Proportion of patients being tested	Puskesmas: 9%; Class C hospitals: 18%
Probability of nothing abnormal detected	CBC: 21%; CBC & smear: 12%; Smear: 22%
Proportion of patients referred to next referral stage	Puskesmas: 45%; Class C hospitals: 68%; Class B hospitals: 83%; Class A hospitals: 30%
Average time between consultations	1.3 weeks
Average time between diagnosis and first treatment response assessment	2.3 weeks
Diagnostics accuracy	Morphology: 78%; Flow cytometry: 95%
Treatment response rates	65–75%
Probability of death if untreated	20–95% across 16 weeks
Diagnostics cost	CBC: IDR137,500; Smear: IDR175,000; Morphology & cytochemical test: IDR450,000; Flow cytometry: IDR933,300
Treatment cost	AML: IDR100 million; ALL: IDR60 million

Local data were used to inform distribution of different healthcare facilities[3] [first consultation: 89% puskesmas, 11% class C hospitals; referral from puskesmas: 81% class C hospitals, 19% class B hospitals] and global peer-reviewed data were used for classification accuracy of morphology and cytochemical test[4] [AML: 92%; ALL: 45%].

Figure 1: Overview of current patient referral pathway based on morphology diagnosis at class A hospitals

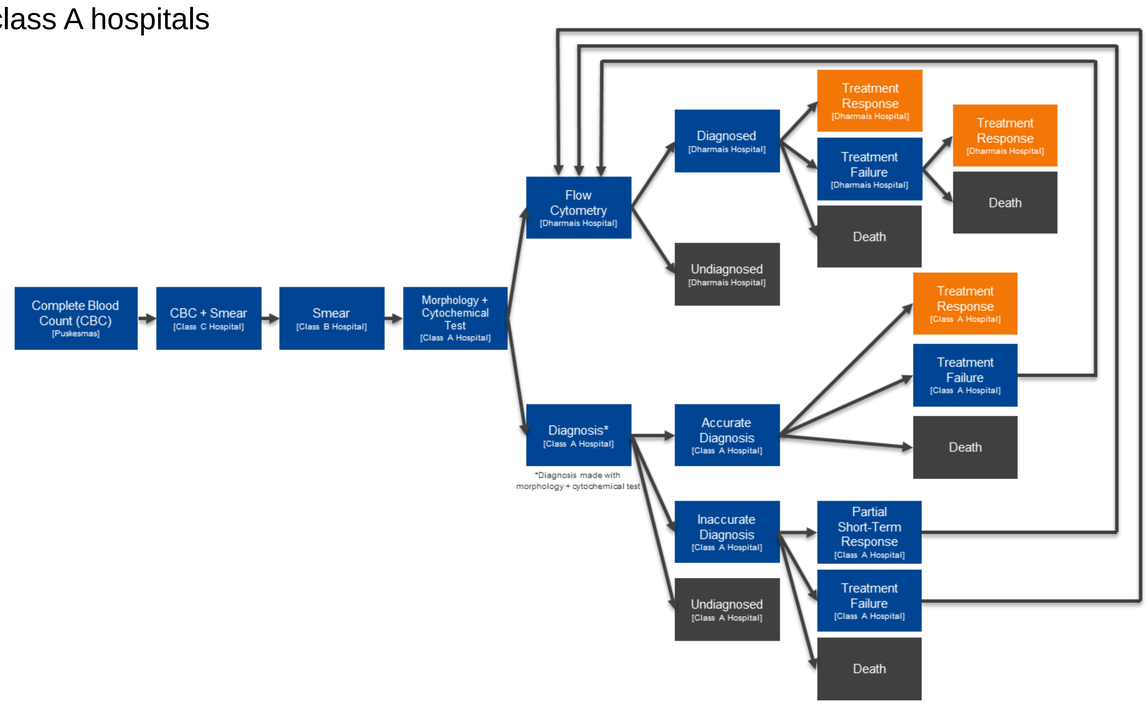
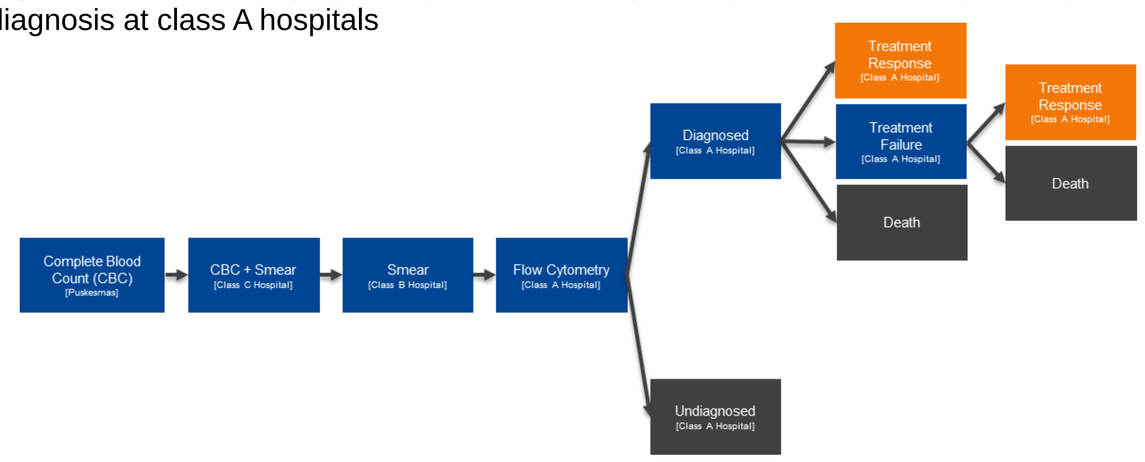


Figure 2: Overview of proposed patient referral pathway based on flow cytometry diagnosis at class A hospitals

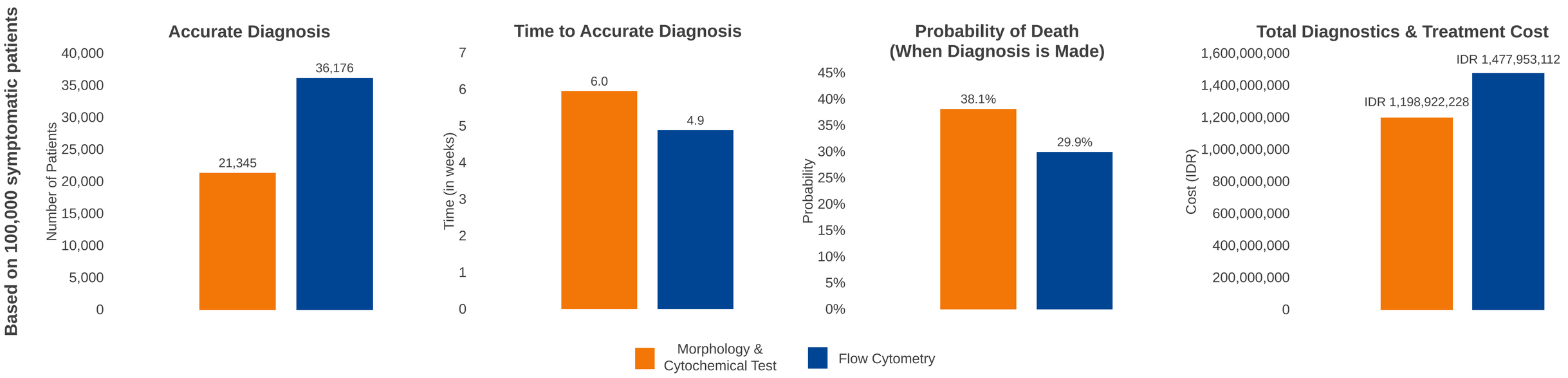


Assumptions: (a) patients can have their first consultation at puskesmas or class C hospitals, (b) patients can be referred to class B or class C hospitals from puskesmas, (c) patients may be sent home with symptomatic treatment (i.e. no test done) at puskesmas or class C hospitals or after nothing abnormal is detected (NAD) from test at each referral stage before class A hospitals [50% lost to follow-up; 50% return for further checks or referral], (d) patients with NAD can return to the referral pathway once and (e) patients will respond to the second optimal treatment if the first fails following an accurate diagnosis

Results

With the adoption of flow cytometry, for 100,000 symptomatic patients, the model estimated 14,830 more patients receiving accurate diagnosis and 5,580 more patients achieving treatment response. Average time to diagnosis can be shortened by one week and average probability of death can be reduced by 22% (**Figure 3**). On average, additional IDR406,700 may be required for each patient's diagnosis but IDR682,300 can be saved from treatment. Overall, IDR110 million can be avoided from unnecessary treatment due to morphological inaccuracies. Total diagnostics and treatment cost is estimated to increase from IDR1,199 to IDR1,478 billion as more patients are being diagnosed and treated (**Figure 3**).

Figure 3: Comparison of clinical and economic outcomes (i.e. number of accurate diagnosis, time to accurate diagnosis, probability of death when accurate diagnosis is made, diagnostics cost and treatment cost) between current pathway (morphology & cytochemical test) and proposed pathway (flow cytometry)



Conclusions

With flow cytometry, more patients can be diagnosed accurately and treated appropriately earlier, thus improving acute leukemia survival. Cost savings can be expected due to reduction of unnecessary treatment.

Conflict of Interest
No potential conflict of interest was reported by the authors.

BD Veeva Vault Ref. No. 21090 - 2020

References

[1]Global Cancer Observatory. Indonesia 2018. Retrieved from https://gco.iarc.fr/today/data/factsheets/populations/360-indonesia-fact-sheets.pdf
[2]Sastroasmoro S. Brief report on "reassessment" of health technology in UHC setting: Indonesia experience. 2019 HTAi Asia Policy Forum; Hanoi, Vietnam; 2019
[3]BPS-Statistics Indonesia. Statistical Yearbook of Indonesia 2018. Retrieved from https://www.bps.go.id/publication/2018/07/03/5a963c1ea9b0fed6497d0845/statistik-indonesia-2018.html
[4]Sengar *et al*. Acute leukemia: Diagnosis improved by flow cytometry in addition to morphology. Asia-Pac J Clin Oncol 2009;5:55–65

Virtual 2020 International Society for Pharmacoeconomics and Outcomes (ISPOR) Asia Pacific Conference; 14–16 September 2020