

# Evaluation of Efficacy, Safety, and Prognostic Value of Induction Chemotherapy in Patients with Acute Myeloid Leukemia: An Updated Meta-Analysis of a 5-Year Study

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Received: 27, Aug, 2024

Accepted: 02, Mar, 2025

## ABSTRACT

Acute Myeloid Leukemia (AML) is a type of cancer that affects the bone marrow and blood. This study aims to conduct a five-year update on induction chemotherapy's efficacy, safety, and prognostic value in patients with AML.

Based on the PRISMA 2020 guidelines, a systematic search was performed on online databases for relevant studies on complete remission with incomplete hematologic response (CRi), complete remission (CR), adverse events, and overall survival. The articles obtained were observational studies that met the inclusion and exclusion criteria. The quality of the studies was assessed using the Revised Cochrane's risk-of-bias tool. The analysis was conducted using Review Manager 5.4 and R Statistical Software 3.3.

Thirteen clinical trial studies, involving 1,863 participants, were included in this survey. Based on the analysis, the CRi and CR levels, where each was obtained as a whole at 9% (random effect; 95%CI 6-13%; heterogeneity;  $\tau^2 < 0.12$ ;  $I^2 = 35\%$ ), and 56% (random effect; 95%CI 43-69%; heterogeneity;  $\tau^2 < 0.01$ ;  $I^2 = 88\%$ ). Gastrointestinal side effects, hepatotoxicity, nephrotoxicity, cardiotoxicity, and infection after induction chemotherapy in AML patients overall were 22% (random effect; 95%CI 10-44%; heterogeneity;  $\tau^2 < 0.01$ ;  $I^2 = 89\%$ ), 8% (random effect; 95%CI 5-11%; heterogeneity;  $\tau^2 = 0.62$ ;  $I^2 = 0\%$ ), 15% (random effect; 95%CI 4-44%; heterogeneity;  $\tau^2 < 0.01$ ;  $I^2 = 89\%$ ), 7% (random effect; 95%CI 5 - 11%; heterogeneity;  $\tau^2 < 0.01$ ;  $I^2 = 76\%$ ), and 20% (random effect; 95%CI 13-30%; heterogeneity;  $\tau^2 < 0.01$ ;  $I^2 = 76\%$ ). Overall survival was 57% (random effect; 95%CI 43-71%; heterogeneity;  $\tau^2 < 0.01$ ;  $I^2 = 86\%$ ). Peter's test showed a significant risk of publication bias. Induction chemotherapy is effective and improves outcomes in AML patients.

**Keywords:** Acute myeloid leukemia (AML); Efficacy; Induction chemotherapy; Prognosis

## INTRODUCTION

Acute myeloid leukemia (AML) is a type of cancer that affects the bone marrow and blood. It is characterized by abnormal growth of white blood cells, interfering with the production of normal blood cells. Acute myeloid leukemia originates in the bone marrow, where immature blood-forming cells undergo abnormal proliferation. Leukemia cells proliferate rapidly, replacing normal cells, causing

symptoms such as anemia, susceptibility to infections, and a tendency for the patient to bleed<sup>1,2</sup>. The incidence of AML can vary significantly in different regions of the world. Approximately 80% of patients with acute leukemia suffer from AML, as one of the most common forms of the disease in adults in the field of hemato-oncology. With a median age of diagnosis of 68 years in adults, acute myeloid leukemia is a disease that primarily affects

the elderly. In the last three decades, there has been a 46% increase in the number of new leukemia cases diagnosed each year worldwide. The two leading causes are aging and the increase in secondary leukemia caused by the extensive use of cytotoxic therapy. Over the last three decades, there has been a constant annual decrease in the incidence of all leukemias by 0.93%. However, there has been a 15% increase in the frequency of AML and a 27% increase in the percentage of AML patients with leukemia overall<sup>3</sup>.

Induction chemotherapy is the cornerstone of AML treatment. The initial phase of therapy aims to induce remission by eliminating leukemia cells from the bone marrow and peripheral blood. The primary goal of induction chemotherapy is to achieve complete remission, defined as the absence of visible leukemia cells in the bone marrow, normalization of blood counts, and resolution of symptoms<sup>4</sup>. Induction chemotherapy usually involves an intensive combination chemotherapy regimen. The most common induction regimen used for AML is the "7+3" regimen, which consists of Cytarabine (Ara-C) given as a continuous infusion for seven days and an anthracycline (such as Daunorubicin or Idarubicin) given as an intravenous infusion for AML for three days. Other intensive regimens may include high-dose Cytarabine or adding different agents, such as Fludarabine or Gemtuzumab Ozogamicin (Mylotarg)<sup>5</sup>.

The success of induction chemotherapy in AML depends on several factors, including patient age, performance status, cytogenetic and molecular abnormalities, and response to initial treatment. Although many patients achieve remission with induction chemotherapy, the risk of relapse remains significant, especially in patients with poor prognostic factors<sup>6</sup>. Induction chemotherapy for AML is associated with significant side effects, including myelosuppression (low blood cell count), increased risk of infection and bleeding, nausea, vomiting, mucositis, hair loss, and fatigue. Supportive care measures are essential to manage these side effects and minimize treatment-related complications<sup>3</sup>. Several previous studies have evaluated the efficacy and safety outcomes of induction chemotherapy in AML, although these

outcomes are still inconsistent. Therefore, this meta-analysis study aims to conduct a five-year updated evaluation of the efficacy, safety, and prognostic value of induction chemotherapy in patients with acute myeloid leukemia.

## MATERIALS AND METHODS

This systematic review and meta-analysis identified, assessed, and interpreted all findings related to the scientific topic. The authors used the PICO (Population, Intervention, Comparison, Outcome, Studies) strategy to identify all relevant studies. All systematic search procedures were conducted based on the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines in 2020.

### Study selection

The studies used in this review are all study articles from online databases, including Medline, EMBASE, Web of Science, Cochrane Library, and Google Scholar, which evaluate induction chemotherapy's effectiveness and prognostic value in patients with acute myeloid leukemia (AML). The effectiveness of therapy is assessed through the parameters of complete remission with incomplete hematologic recovery (CRi) and complete remission (CR). Meanwhile, the prognosis of patients after induction chemotherapy is assessed by evaluating adverse effects and overall survival (OS). The population of this study was AML patients who had undergone induction chemotherapy. Studies were not included if (1) Studies with a population undergoing additional therapy other than induction chemotherapy, (2) studies with a follow-up period of less than one year, (3) studies that did not clearly state the effectiveness or prognosis outcomes, (4) observational study design.

### Literature searching

The search for relevant literature or studies uses several keywords from the PICOS development to obtain maximum search findings. In the study search process, the author's first step is determining keywords using Medical Subject Headings (MeSH). After selecting keywords using MeSH, a research journal search technique uses advanced search,

bibliographic search, and Boolean operators (AND, OR, and NOT) on keywords arranged according to research topics. The search terms used are (effectiveness) AND (prognostic) AND (acute myeloid leukemia) AND ((chemotherapy) OR (induction chemotherapy)).

#### Data extraction and study quality assessment

Overall, this study used critical appraisal to assess the quality of articles that could be included in the systematic review. The authors performed data extraction independently. The quality assessment of studies was carried out using RoB 2: A revised Cochrane risk-of-bias tool for randomized trials, which was grouped into three assessment groups (high, low, or unclear/concerning risk of bias) for each element of the five domains (selection, performance, attrition, reporting, and others). If the interpretation obtained as a whole is good enough, the article is declared to meet the criteria and included in the inclusion criteria, and vice versa.

#### Data analysis

Data analysis was conducted by systematically integrating and describing all data to draw conclusions. The data consisted of research characteristics (name of primary author, year of publication, and study location), population characteristics, measurement methods, measurement parameters, and main results. Data were presented in a table (synthesis matrix) to facilitate analysis. Quantitative analysis was conducted using single proportion analysis to determine the overall patient survival rate using Review Manager v.5.4 software and R Statistical Software v.3.3. Heterogeneity was assessed using the I-square and T-square tests. Significant heterogeneity values were indicated using a random effect model in the analysis. The risk of publication bias was evaluated using a quantitatively qualitative funnel plot approach and Peter's test. The significant p-value accepted was <0.05.

## RESULT

### Study searching

In the study search process, 12,450 articles were obtained from online databases (PubMed,

ScienceDirect, Cochrane, and Google Scholar). Eleven thousand two hundred fifty-five articles were obtained after removing duplicates using computer software (Citation Manager). In the title and abstract screening process, 56 articles were obtained that could be accessed and assessed for eligibility. In addition, 43 articles were excluded because they did not have complete or relevant data on survival rate outcomes, resulting in qualitative (systematic review) and quantitative (meta-analysis) analyses using 13 included studies. The study search flow using the PRISMA guidelines is described as follows (Figure 1).

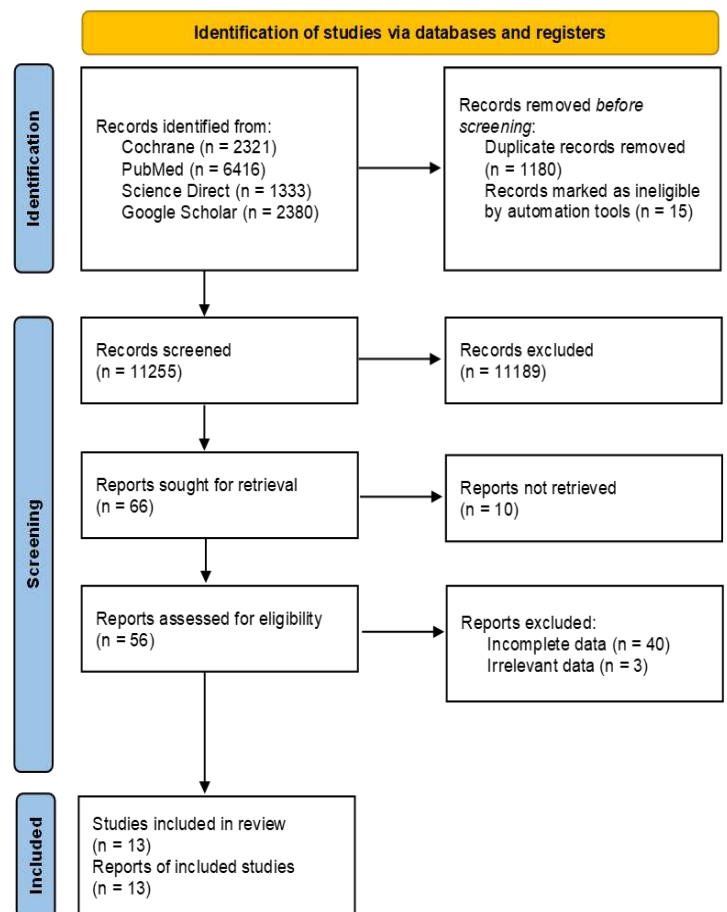


Figure 1. PRISMA Flowchart

**Study characteristics**

The review included 13 studies, with the majority originating from the United States (8) and China (2). All studies used a clinical trial design, with daunorubicin being the most common intervention.

The total sample population of all studies reached 1204 participants in the intervention group and 1863 participants overall. Overall study characteristic data are described in Table 1.

**Table 1.** Study characteristics

Author, year	Study design	Country	Type of induction chemotherapy		Sample population		
			Intervention	Comparator	Intervention	Comparator	Total
Gill dkk., 2020 <sup>7</sup>	<i>Clinical Trial</i>	China	Clofarabine, cytarabine, mitoxantrone	N/R	52	N/R	52
Guolo dkk., 2020 <sup>8</sup>	<i>Clinical Trial</i>	Italia	Daunorubicin, cytarabine	N/R	71	N/R	71
Issa dkk., 2020 <sup>9</sup>	<i>Clinical Trial</i>	USA	Daunorubicin, cytarabine	N/R	56	N/R	56
Kadia dkk., 2021 <sup>10</sup>	<i>Clinical Trial</i>	USA	Venetoclax, cladribine, idarubicin, cytarabine	N/R	50	N/R	50
Muresan dkk., 2021 <sup>11</sup>	<i>Clinical Trial</i>	Netherland	Gemtuzumab, ozogamicin, daunorubicin, cytarabine	Daunorubicin, cytarabine	135	136	271
Ravandi dkk., 2019 <sup>12</sup>	<i>Clinical Trial</i>	USA	Idarubicin, cytarabine, nivolumab	N/R	44	N/R	44
Russel dkk., 2024 <sup>13</sup>	<i>Clinical Trial</i>	USA	FLAG-Ida	Daunorubicine, Ara-C	522	523	1045
Sanchez dkk., 2021 <sup>14</sup>	<i>Clinical Trial</i>	Spain	Selinexor, FLAG-Ida	N/R	12	N/R	12
Saygin dkk., 2020 <sup>15</sup>	<i>Clinical Trial</i>	USA	Lenalidomide, idarubicine, cytarabine	N/R	33	N/R	33
Sweet dkk., 2020 <sup>16</sup>	<i>Clinical Trial</i>	USA	Selinexor, daunorubicin, cytarabine	N/R	21	N/R	21
Wieduwilt dkk., 2019 <sup>17</sup>	<i>Clinical Trial</i>	USA	Daunorubicin, cytarabine	N/R	25	N/R	25
Zeidner dkk., 2021 <sup>18</sup>	<i>Clinical Trial</i>	USA	Alvocidib, daunorubicin, cytarabine	N/R	32	N/R	32
Zhang dkk., 2022 <sup>19</sup>	<i>Clinical Trial</i>	China	Idarubicine, cytarabine	N/R	151	N/R	151

\*N/R; not reported

**Table 2.** Study outcome

Author, year	Study outcome	Risk of Bias
Gill dkk., 2020 <sup>7</sup>	The treatment in this study was highly effective for refractory/relapsed AML, and its efficacy was unaffected by high-risk karyotypes and genetic mutations.	<i>Low risk</i>
Guolo dkk., 2020 <sup>8</sup>	CPX is an effective regimen for high-risk AML patients and may improve HSCT outcomes.	<i>Low risk</i>
Issa dkk., 2020 <sup>9</sup>	CPX-351 can be safely administered to patients with AML with risk features considered at high risk for death with intensive chemotherapy.	<i>Low risk</i>
Kadia dkk., 2021 <sup>10</sup>	Venetoclax added to CLIA is safe and effective in newly diagnosed AML and high-risk MDS.	<i>Low risk</i>
Muresan dkk., 2021 <sup>11</sup>	MCMs are showing a promising outcome resulting in long-term survival in acute myeloid leukemia patients.	<i>Low risk</i>
Ravandi dkk., 2019 <sup>12</sup>	Adding nivolumab to idarubicin+cytarabine induction therapy has shown promising results and is safe in AML patients, especially in pediatric patients.	<i>Low risk</i>
Russel dkk., 2024 <sup>13</sup>	LAG-Ida 1 GO significantly reduced recurrence, although it was not significant in producing OS improvement.	<i>Low risk</i>
Sanchez dkk., 2021 <sup>14</sup>	Combining selinexor with FLAG-Ida in adult patients with R/R AML demonstrated acceptable tolerability and antileukemic solid efficacy.	<i>Low risk</i>
Saygin dkk., 2020 <sup>15</sup>	The combination chemotherapy of lenalidomide and cytarabine/idarubicin has clinical activity in patients with R/R AML.	<i>Low risk</i>
Sweet dkk., 2020 <sup>16</sup>	Selinexor plus 7+3 is a safe regimen for patients with newly diagnosed low-risk AML.	<i>Low risk</i>
Wieduwilt dkk., 2019 <sup>17</sup>	Panobinostat at biologically relevant doses was well tolerated when given briefly before and during "7+3" induction to elderly patients with newly diagnosed disease.	<i>Low risk</i>
Zeidner dkk., 2021 <sup>18</sup>	Alvocidib administration before 7+3 induction was tolerated, feasible, and showed encouraging clinical activity in newly diagnosed unfavorable-risk cytogenetics.	<i>Low risk</i>
Zhang dkk., 2022 <sup>19</sup>	Optimization of induction chemotherapy with idarubicin and cytarabine according to D5-PBCR is feasible in patients with newly diagnosed AML.	<i>Low risk</i>

**Quantitative analysis**

Next, a quantitative analysis was conducted to determine the effectiveness and prognosis of

patients with AML after induction chemotherapy in all included studies. The analysis is described below.

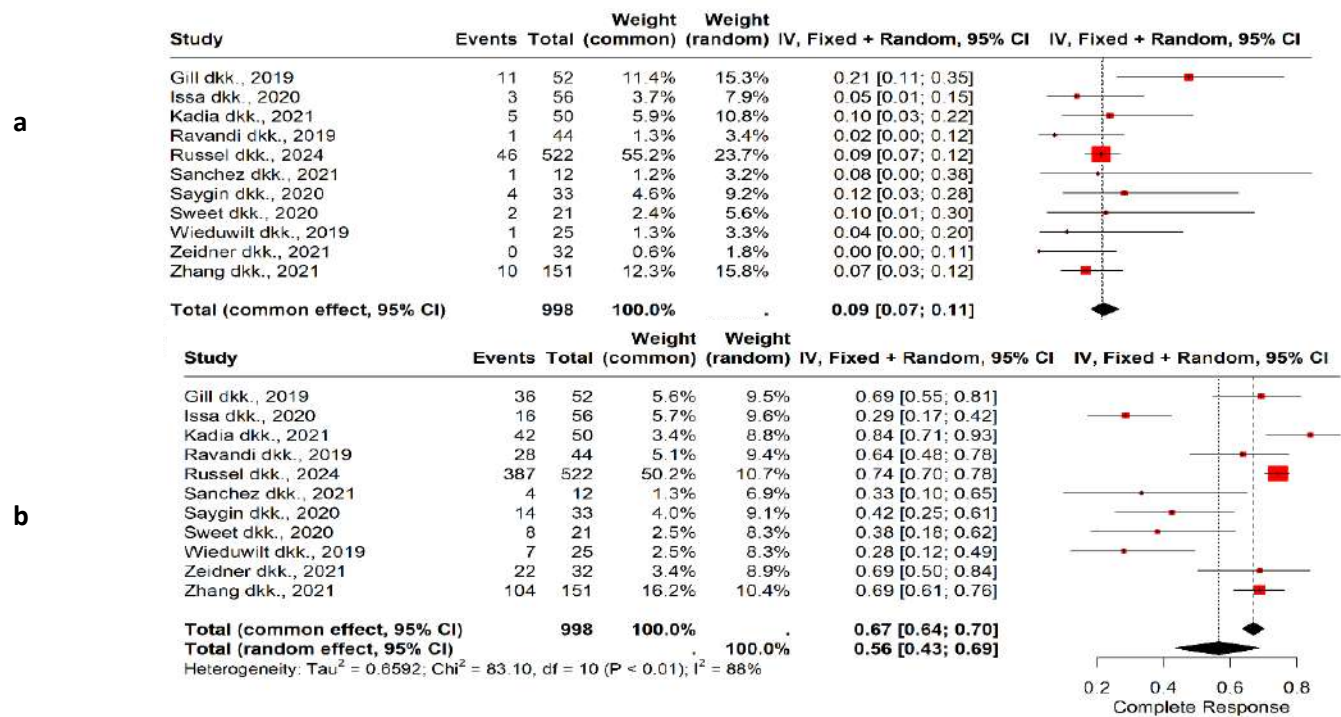


Figure 2. (a) Forest plot analysis of complete remission with incomplete hematologic recovery, and (b) complete remission after induction chemotherapy in AML patients.

A total of 12 studies were included in the analysis of therapeutic response consisting of CRi and CR, where each overall was obtained at 9% (random effect;

95%CI 6-13%; heterogeneity;  $\tau^2 < 0.12$ ;  $I^2 = 35\%$ ), 56% (random effect; 95%CI 43-69%; heterogeneity;  $\tau^2 < 0.01$ ;  $I^2 = 88\%$ ) (Figure 2)



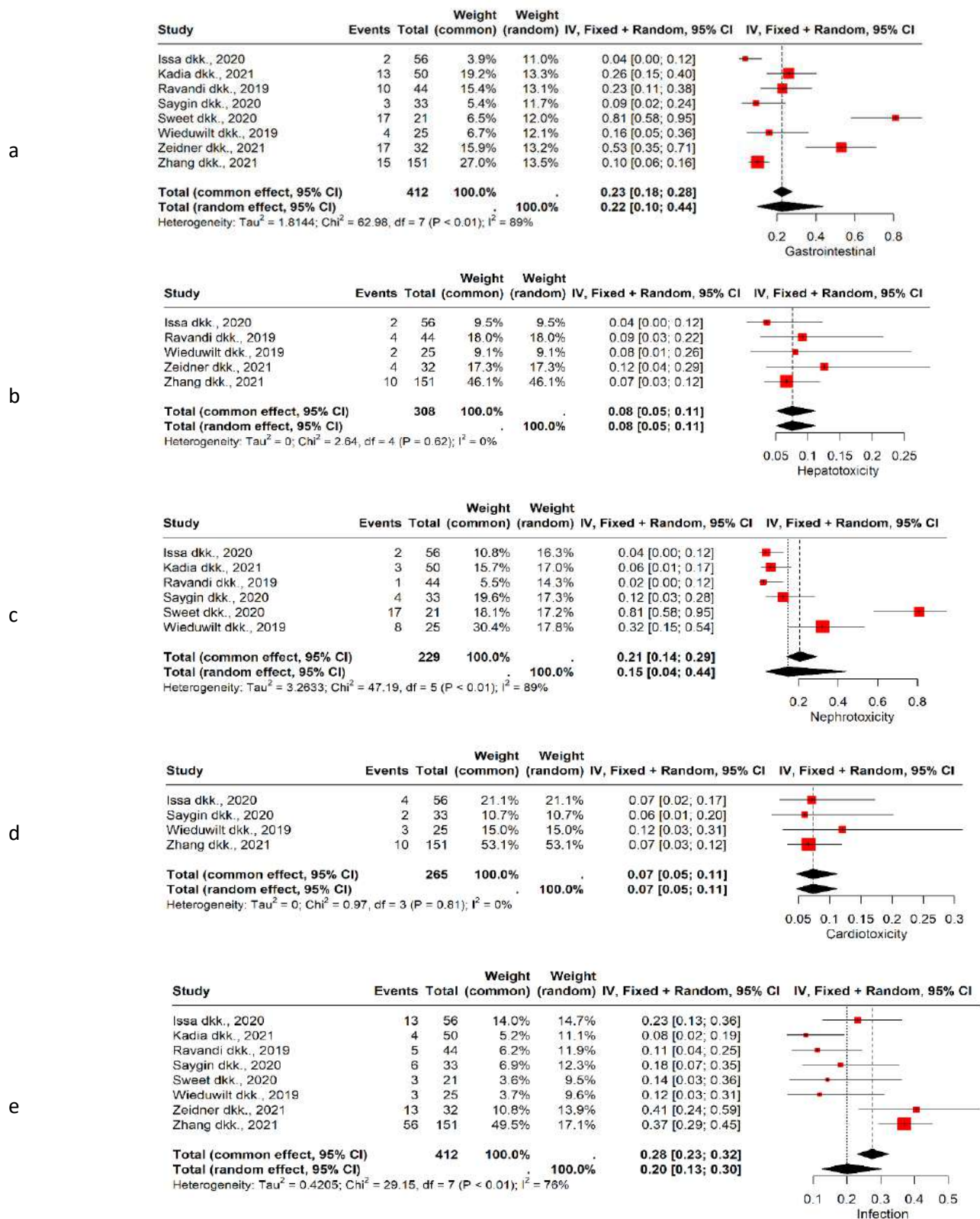


Figure 3. Forest plot analysis of adverse events including gastrointestinal (a), hepatotoxicity (b), nephrotoxicity (c), cardiotoxicity (d), and infection (e) after induction chemotherapy in AML patients.

A total of 9 studies were included in the adverse event analysis, where the percentage of gastrointestinal side effects, hepatotoxicity, nephrotoxicity, cardiotoxicity, and infection after induction chemotherapy in AML patients as a whole was 22% (random effect; 95%CI 10-44%; heterogeneity;  $\tau^2 < 0.01$ ;  $I^2 = 89\%$ ), 8% (random effect;

95%CI 5-11%; heterogeneity;  $\tau^2 = 0.62$ ;  $I^2 = 0\%$ ), 15% (random effect; 95%CI 4-44%; heterogeneity;  $\tau^2 < 0.01$ ;  $I^2 = 89\%$ ), 7% (random effect; 95%CI 5-11%; heterogeneity;  $\tau^2 < 0.01$ ;  $I^2 = 76\%$ ), and 20% (random effect; 95%CI 13-30%; heterogeneity;  $\tau^2 < 0.01$ ;  $I^2 = 76\%$ ) (Figure 3)

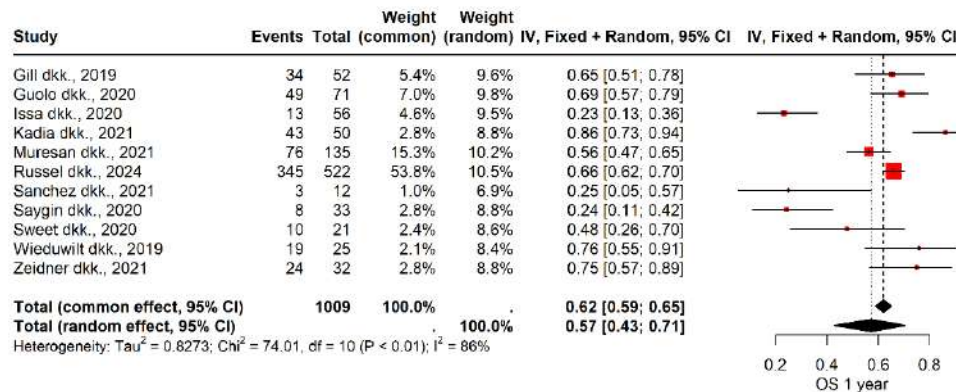


Figure 4. Forest plot analysis of overall survival within 1 year after induction chemotherapy in AML patients

A total of 11 studies were included in the overall survival (OS) analysis at 1 year, which found that the overall OS rate was 57% (random effect; 95%CI 43-71%; heterogeneity;  $\tau^2 < 0.01$ ;  $I^2 = 86\%$ ) (Figure 4)

### Publication bias

Publication bias analysis was performed using Peter's test, which showed that complete remission with incomplete hematologic recovery, complete remission, gastrointestinal, and nephrotoxicity parameters had a significant risk of experiencing publication bias ( $p < 0.05$ ). The results of the publication bias analysis are described in Table 3.

Table 3. Publication bias analysis using Peter's test

No	Parameter	SE	p
1	Complete remission with incomplete hematologic recovery	10.86	0.663
2	Complete remission	10.79	0.021
3	Gastrointestinal	26.37	0.045
4	Hepatotoxicity	14.84	0.338
5	Nephrotoxicity	23.00	0.003
6	Infection	18.11	0.152
7	One-year overall survival	13.64	0.310



## DISCUSSION

Induction chemotherapy is an essential initial phase of treatment for many types of cancer, including AML. The primary goal of induction chemotherapy is to rapidly reduce the burden of cancer cells in the body, achieving complete remission. In AML, induction chemotherapy aims to eliminate leukemia cells from the bone marrow and peripheral blood, thereby restoring normal hematopoiesis. Achieving a complete response or remission is an important prognostic factor in AML, associated with improved clinical outcomes and therapy efficacy. Patients who achieve complete remission have a greater chance of long-term survival than those who do not<sup>20</sup>.

This meta-analysis found that induction chemotherapy drugs in AML patients have quite good efficacy values. This meta-analysis found complete remission as the primary outcome, reaching 56%, with cumulative results reaching 67%. The results of this study are from several previous studies. A survey conducted by Owattanapanich et al. compared the efficacy and toxicity of Idarubicin versus high-dose Daunorubicin for induction chemotherapy in adult AML patients. Based on the study results, it was concluded that Idarubicin and high-dose Daunorubicin are effective induction chemotherapy agents for adult AML patients, with reasonable complete remission rates<sup>21</sup>. Although Idarubicin has a lower risk of mucositis compared to high-dose Daunorubicin, both regimens showed similar rates of treatment-related death, infection, and cardiotoxicity<sup>22</sup>.

The results of this study are supported by research conducted by Norsworthy et al., which aims to assess the response rate and Overall Survival (OS) in newly diagnosed AML patients by assessing the response rate (complete remission and complete remission with incomplete hematologic recovery), and OS outcomes. This study found a moderate trial-level relationship between response rate (complete remission and complete remission with incomplete hematologic recovery) and OS in patients receiving intensive chemotherapy to treat newly diagnosed AML<sup>23</sup>.

A study conducted by Wang et al. aimed to compare the efficacy and safety of two anthracycline drugs, Idarubicin and Daunorubicin, when combined with Cytarabine for induction therapy in AML, found no significant difference in complete remission rates between the Idarubicin and Daunorubicin induction regimens. There was no significant difference in treatment-related mortality or severe adverse event rates between the two treatment arms. The study concluded that Idarubicin and Daunorubicin, combined with Cytarabine, are effective induction therapy options for AML, with comparable efficacy and safety profiles. The choice between Idarubicin and Daunorubicin may depend on factors such as drug availability, cost, and individual patient characteristics<sup>24</sup>.

Induction chemotherapy for AML can be associated with a variety of side effects, which can significantly impact patient well-being and treatment outcomes. These side effects include the risk of infection, gastrointestinal symptoms, cardiotoxicity, hepatotoxicity, and nephrotoxicity. In this meta-analysis, the incidence of gastrointestinal symptoms was 22%. Induction chemotherapy for AML can cause a variety of gastrointestinal symptoms due to the effects of chemotherapy that interfere with the function of other normal cells<sup>25</sup>. Chemotherapy-induced nausea and vomiting are some of the most common gastrointestinal symptoms experienced by AML patients with induction chemotherapy therapy. Chemotherapy drugs can stimulate the vomiting center in the brain, causing nausea and vomiting. Antiemetic drugs are often prescribed to help manage these side effects and improve patient comfort<sup>26</sup>. Chemotherapy-induced mucositis is characterized by inflammation and ulceration of the mucous membranes lining the mouth, throat, and digestive tract. Mucositis can cause pain, difficulty swallowing (dysphagia), and mouth ulcers, making it difficult to eat and increasing susceptibility to infection. Some chemotherapy agents used in AML induction regimens can cause diarrhea as a side effect. Diarrhea can be acute or chronic and can lead to dehydration and electrolyte imbalance if not appropriately managed. Antidiarrheal medications,

fluid replacement, and dietary changes may be recommended to relieve symptoms. Chemotherapy-induced gastrointestinal symptoms such as nausea, vomiting, mucositis, and diarrhea can cause decreased appetite, anorexia, and weight loss in AML patients undergoing induction chemotherapy<sup>27</sup>.

In this meta-analysis study, the incidence of side effects as a risk of infection was 20%. Induction chemotherapy for AML can increase the risk of infection due to its myelosuppressive effects, which interfere with the normal function of the bone marrow and immune system. Induction chemotherapy often causes a significant decrease in neutrophils, known as neutropenia<sup>28</sup>. Fever during neutropenia is a common complication of induction chemotherapy in AML patients. It is considered a medical emergency requiring immediate evaluation and treatment with broad-spectrum antibiotics to cover many potential pathogens<sup>29</sup>. Empiric antibiotic therapy is initiated immediately after the onset of fever in neutropenic patients, even without an identified infection, to reduce the risk of serious complications such as sepsis<sup>30</sup>. Patients undergoing induction chemotherapy for AML are also at risk for opportunistic infections, which are caused by pathogens that do not usually cause disease in individuals with intact immune systems but can cause severe infections in patients with weakened immune systems<sup>31</sup>.

Induction chemotherapy for AML has the potential to cause cardiotoxicity, especially with the use of anthracycline drugs such as Idarubicin and Daunorubicin, which are commonly included in induction regimens. Anthracycline chemotherapy drugs are known to cause dose-dependent cardiotoxicity, characterized by damage to the heart muscle (cardiomyopathy) and the potential for the development of heart failure or arrhythmias. Anthracycline-induced cardiotoxicity can occur acutely during treatment or appear years after completion of chemotherapy<sup>21</sup>. The exact mechanism of anthracycline-induced cardiotoxicity is not fully understood but is thought to involve multiple pathways, including oxidative stress, mitochondrial dysfunction, and cardiac cell membrane disruption. Anthracyclines can induce the formation of reactive oxygen species, which results

in oxidative damage to cardiac cells and impaired cardiac function. Given the potential for cardiotoxicity, cardiac monitoring is essential for AML patients undergoing induction chemotherapy with anthracycline-containing regimens. Baseline cardiac function assessment, including echocardiography or cardiac MRI, may be performed before initiating chemotherapy. Serial monitoring of cardiac function during and after treatment may help detect early signs of cardiotoxicity and guide management decisions<sup>32</sup>.

In this meta-analysis study, the incidence of side effects in nephrotoxicity was 15% of the total sample of included studies. Induction chemotherapy for AML has the potential to cause nephrotoxicity, which is kidney damage or dysfunction due to the toxic effects of chemotherapy agents. Certain chemotherapy drugs used in AML induction regimens have the potential to cause nephrotoxicity. Although not all chemotherapy agents used in AML induction chemotherapy are directly nephrotoxic, some drugs or their metabolites can affect kidney function. Tumor lysis syndrome (TLS) is a potential complication of induction chemotherapy in AML, especially in patients with a high tumor burden. Tumor lysis syndrome occurs when many leukemia cells are rapidly destroyed, releasing intracellular contents such as potassium, phosphate, and nucleic acids into the bloodstream<sup>33</sup>. These substances can overwhelm the kidneys' ability to excrete them, leading to acute kidney injury (AKI) and electrolyte abnormalities. Nausea, vomiting, diarrhea, and decreased oral intake due to chemotherapy-induced gastrointestinal symptoms can lead to dehydration and volume depletion in AML patients undergoing induction chemotherapy. Dehydration can compromise kidney function and increase the risk of nephrotoxicity. Specific chemotherapy agents used in AML induction regimens, such as high-dose Cytarabine, can cause direct kidney injury<sup>21,34</sup>.

In this meta-analysis study, hepatotoxicity side effects were found in 8% of the total study samples in the included studies. Induction chemotherapy for AML has the potential to cause hepatotoxicity, which is liver damage or dysfunction due to the toxic effects of chemotherapy agents. Certain chemotherapy drugs used in AML induction regimens have the

potential to cause hepatotoxicity. These drugs may include anthracyclines (such as Idarubicin and Daunorubicin), Cytarabine, and other agents commonly used to treat AML<sup>35</sup>. Chemotherapy drugs can directly damage liver cells, causing hepatotoxicity. Hepatotoxicity can manifest as elevated liver enzymes (e.g., Alanine Transaminase [ALT], Aspartate Transaminase [AST]) and bilirubin levels, indicating liver injury or dysfunction. Chemotherapy agents are metabolized and cleared by the liver, which can further increase the risk of hepatotoxicity. Liver damage can interfere with the metabolism and clearance of chemotherapy drugs, leading to increased drug exposure and potential toxicity. Tumor Lysis Syndrome, a possible complication of induction chemotherapy in AML, can also affect liver function. Tumor Lysis Syndrome occurs when large numbers of leukemia cells are rapidly destroyed, releasing intracellular contents into the bloodstream. These substances can overwhelm the liver's capacity to metabolize and excrete them, leading to liver dysfunction and elevated liver enzymes<sup>21,33</sup>.

This meta-analysis study still has several limitations, such as the analysis still using a descriptive design due to the very heterogeneous inclusion studies to standardize the treatment and control groups to conduct analytical studies. This study also did not carry out design control on the age group of the study sample, so the population used in this study was not homogeneous, which may affect the results of the inclusion studies and the reported clinical outcomes.

## CONCLUSION

Based on the analysis results, it can be concluded that the effectiveness of induction chemotherapy in AML patients is quite good, as reflected by the parameters of complete remission with incomplete hematologic recovery and full remission, which are 9% and 56%, respectively. Furthermore, the parameters of gastrointestinal side effects, hepatotoxicity, nephrotoxicity, and infection after induction chemotherapy in AML patients were obtained at 22%, 8%, 15%, and 20%, respectively. Finally, the predictive value of induction chemotherapy in AML patients is also quite good, as

reflected by the overall survival (OS) in 1 year of 57%. Further research is needed regarding the comparison of induction chemotherapy with other therapeutic modalities in AML patients.

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