

Comparing The Efficacy of Different Antibiotic Regimens in The Treatment of Community-Acquired Pneumonia Based on Clinical Outcomes.

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ABSTRACT

Background: Community-acquired pneumonia is one of the most important causes for the development of morbidity and hospitalization in the world and, hence, requires timely and effective antibiotics therapy. This study was undertaken to compare the efficacy, clinical outcomes, and safety of three different antibiotic regimens in patients suffering from CAP.

Methodology: This study examined the 150 patients suffering from CAP, with fifty patients per group: Regimen A, Regimen B, and Regimen C. Important parameters observed include normalization of vital signs, clinical improvement, clinical stability, time interval to clinical improvement, length of hospital stay, side effects, mortality, and thirty-day readmission rates. Data were analyzed and tested for statistical significance to show the efficacy of the different regimens.

Results: All three regimens showed complete stability within 24 hours, with overall clinical improvement rates at 84.0%, with Regimen C showing the greatest improvement, followed by Regimen B (72.0%) and Regimen A (64.0%). This shows that although the three regimens have similar effectiveness on clinical improvement, for quicker symptom relief and clinical recovery, Regimen C emerges as the best in this study. Mean duration of hospital stay was also similar for all, ranging from 7–7.62 days, and statistically not significant ($p > 0.00001$). There was no death reported in any group. Side effects profile varied, with diarrhea being the most common adverse effect in Regimen C (21), whilst nausea was seen most commonly in Regimen A (20).

Conclusion: Out of all three antibiotic regimens, the choice of regimen resulted in similar efficacy in the treatment of community-acquired pneumonia, with 100% clinical stability, no mortality, and comparable lengths of stay. Regimen C had the quickest resolution of fever but higher incidence of diarrhea, whereas Regimen A demonstrated more rapid improvement in dyspnea. In general, all the regimens were effective with minimal variation in side effects and time to resolution of various other symptoms.

Keywords: Community-acquired pneumonia, Antibiotic regimens, Efficacy, Clinical outcomes, Safety, Comparative study, Hospitalization, Treatment.

1. INTRODUCTION

The impact of community-acquired pneumonia (CAP) on morbidity and mortality continues to be significant on a worldwide scale, especially in respect of the elderly and the immunocompromised. Despite advances in diagnostic techniques and supportive care, the treatment of CAP is still a challenge because of changing patterns of resistance in microorganisms and fluctuating presentations in clinical history. The mainstay of treatment is effective antibiotic therapy, while the key to improving outcomes is its timely application. However, controversy still surrounds the specific choices regarding the optimal antibiotic regimen due to variations in local resistance patterns, comorbid conditions which could impair the activity of antibiotics or impact therapy outcomes, and differential patient responses.[1,2].

According to the most recent treatment guidelines, empirical antibiotic therapy according to severity, risk factors, and local antibiograms is adopted. Beta-lactams, macrolides and fluoroquinolones as monotherapy or in combination are some common regimens. Comparative evidence of the clinical efficacy of such regimens is still limited especially in real-world outcomes like symptom resolution, inflammatory marker reduction, length of hospital stay, and readmission rates. More clarity regarding comparative efficacy will inform clinicians in finding the best initial antibiotic options for patients and in improving recovery outcomes.^[3,4]

This research was conducted to evaluate and compare the clinical efficacy of three different antibiotic regimens most frequently utilized in patients with community-acquired pneumonia while being hospitalized. The main criteria for evaluation included the resolution of fever, cough, dyspnea, radiologic improvement, and normalization of inflammatory markers (CRP, procalcitonin, WBC count). Other parameters that were considered for a global assessment included normalization of vital signs, time to clinical improvement, adverse effects, and percentage of 30-day readmission.^[5,6]

This research will generate useful data for evidence-based prescribing for CAP by systematically comparing the outcome among Regimens A, B, and C. The aim is not only to ascertain differences in clinical efficacy but also to highlight safety profiles and recovery pathways of the regimens. Such information can facilitate clinicians' choice of therapy, according to the requirements of each patient, thereby increasing care quality for patients suffering from this very commonplace but potentially grave infection.^[7,8]

AIM:

To compare the efficacy of different antibiotic regimens in the treatment of community-acquired pneumonia based on clinical outcomes.

OBJECTIVES:

To Evaluate and compare the clinical improvement among different antibiotic regimens.

To Evaluate and compare the clinical stability among different antibiotic regimens.

To evaluate the Time for clinical improvement and length of hospital stay for patients receiving different antibiotic treatments.

To assess the mortality rate within 30 days of initiating antibiotic therapy.

To analyze the rate of side effects associated with different antibiotic regimens.

METHODOLOGY

Ethical Approval: The study is initiated after the clearance of institutional ethics committee

Study Site: This research was Conducted at a tertiary care hospital in the Pulmonology Department.

Study Duration: The study was conducted for a period of 6 months.

Sample Size: Let's assume some typical values for the other variables. Using the formula, the calculation would look like this,

$Z_2 = 1.96$ (Z-score for 95% confidence level)

$p = 0.5$ (population proportion, assuming a binary variable)

$E_2 = 0.05$ (margin of error, 5%)

$N = 242$ (No of Population)

Now, plug in these values:

$n = [(1.96)^2 \times 0.5 \times (1-0.5) / (0.05)^2] \times [242-1/242]$

$n \approx [3.8416 \times 0.25 / 0.0025] \times [241/242]$

$n \approx 384.16 \times 0.25 \times 0.9959$

$n \approx 150.34$

So, the required sample size n is approximately 150

Sample size was 150. 50 patients were randomly assigned to each antibiotic regimen group (3 groups) to ensure equal distribution. Each group ($n=50$) received a specific regimen, and outcomes were compared.

Study Design: Prospective, Observational, Comparative study

Study Criteria

Inclusion criteria:

Patients aged ≥ 18 years diagnosed with CAP based on clinical and radiological findings.

Patients receiving antibiotic therapy as per hospital protocol.

Patients willing to provide informed consent.

Exclusion criteria:

Patients with hospital-acquired pneumonia (HAP) or ventilator-associated pneumonia (VAP).

Patients with immunodeficiency disorders (e.g., HIV/AIDS, undergoing chemotherapy).

Pregnant or lactating women.

Study Method

This observational, comparative study plans to analyze the effectiveness of different regimens in treating community-acquired pneumonia (CAP). Patients with CAP were included using specific criteria. All baseline demographic, clinical, laboratory, and radiological data were collected. Patients were classified according to the antibiotic regimens they are prescribed. Improvement and stabilization clinically, inflammatory markers (C-reactive protein, Procalcitonin, WBC), length of stay, and adverse effects were recorded after 10 days. Statistical analysis like Chi-square tests, t-tests, and mean comparisons were used to analyze treatment efficacy. Outcomes include time for clinical improvement, time-to-stabilization, and mortality. Ethical clearance was taken along with the patient's confidentiality following Good Clinical Practice guidelines.

Statistical Analysis

After entering the data into a Microsoft Excel spreadsheet, different statistical procedures were used to do statistical analysis and provide frequencies and percentages.

RESULTS**PATIENT CHARACTERISTICS**

PATIENT CHARACTERISTICS		REGIMEN: A	REGIMEN: B	REGIMEN: C
GENDER	FEMALE	24	23	24
	MALE	26	27	26
AGE	<30	10	7	4
	31-40	4	9	14
	41-50	9	7	7
	51-60	12	13	9
	61-70	8	4	5
	>70	7	10	11
AREA OF RESIDENCE	RURAL	24	21	28
	URBAN	26	29	22
SMOKING STATUS	EX-SMOKER	18	20	24
	SMOKER	20	19	12
	NON-SMOKER	12	11	14
ALCOHOL USE	NO	26	26	18
	YES	24	24	32
COMORBIDITIES	DIABETES	5	10	9
	HEART DISEASE	8	9	6

	HYPERTENSION	10	9	10
	CKD	7	4	7
SPUTUM CULTURE: MICRO-ORGANISM	S. PNEUMONIAE	19	30	18
	H. INFLUENZAE	16	10	29
	K. PNEUMONIAE	15	10	3
FAMILY HISTORY OF COMMUNITY ACQUIRED PNEUMONIA	NO	25	17	31
	YES	25	33	19

This table lists the distributions of demographic variables and clinical baseline characteristics for 150 patients allocated to Regimen A, B, C (50 patients in each group). This table summarized that there is equal distribution of gender across these groups. The maximum number of study participants was found in 51 to 60 age groups in A (12 patients) and B(13 patients); while that of Regimen C is reflected in 31-40 years categories which had 14 patients. Most patients came from rural areas in Regimen C (28 patients), compared with the urban majority in Regimen B (29). Generally, smoking was highest in Regimen A (20 smokers) while thinned down with alcohol use where compared in Regimen C (32 patients). Hypertension was the ailment most frequently found amongst them. It showed the following microorganisms: S. pneumoniae, 30 cases in B; H. influenzae, 29 in C, and K. pneumoniae, 15 in A. Speaking of passages, family history of pneumonia was reported by 33 patients in Regimen B.

CLINICAL VALUES: BASELINE AND 10 DAY FOLLOW-UP COMPARISON

CLINICAL VALUES	REGIMEN: A			REGIMEN: B			REGIMEN: C		
	BASE LINE	10 DAY	% CHANGE	BASE LINE	10 DAY	% CHANGE	BASE LINE	10 DAY	% CHANGE
FEVER (YES)	26	12	53.8	23	8	65.2	25	6	76.0
COUGH (YES)	24	10	58.3	17	7	58.8	23	8	65.2
DYSPNEA (YES)	28	13	53.6	24	8	66.7	22	5	77.3
ABNORMAL X- RAY FINDINGS (YES)	29	9	69.0	25	7	72.0	31	5	83.9
SPO2 ABNORMAL (YES)	19	9	52.6	21	9	57.1	20	6	70.0

The table show the clinical baselines and 10-day follow-up values for all three regimens (A, B, and C) regarding key symptoms; namely fever, cough, dyspnea, abnormal X-ray findings, and SPO2 abnormalities. All three regimens are said to be significantly beneficial over the course of 10 days; however, for the majority of the clinical parameters considered, Regimen C consistently shows a higher percentage reduction i.e., fever by 76.0%, dyspnea by 77.3%, abnormal x-ray findings by 83.9%, and SPO2 abnormalities by 70.0% were reduced. Additionally Regimen B indicated some significant reductions, especially cough (58.8%) and abnormal x-ray findings (72.0%). The least lower reductions were revealed in regimen A, with fever and dyspnea proven to reduce by 53.8 and 53.6%, respectively. Therefore, overall Regimen C was considered as the best addressing symptom reduction in the 10-day course.

CLINICAL IMPROVEMENT ASSESSMENT

CLINICAL IMPROVEMENT	REGIMEN: A	REGIMEN: B	REGIMEN: C	P VALUE
NO	18	14	8	>0.00001
YES	32	36	42	
% CLINICAL IMPROVEMENT	64.00%	72.00%	84.00%	

The best clinical improvement is seen with regimen C, which demonstrated positive outcomes in 84.00% of patients with only 8 patients not showing clinical improvement. Regimen B followed right behind with a 72.00% improvement rate, having 14 patients that did not show any clinical improvement. The least improvement is recorded with regimen A at 64.00%, with 18 patients still showing no signs of recovery. There is no significant difference between the observed improvements between the three regimens (χ^2 test, $p > 0.00001$) suggesting that all three regimens show clinical improvement equally, but Regimen C clearly outperformed all others and is likely to stand as the best treatment option amongst the three regimens examined.

C – REACTIVE PROTEIN: BASELINE AND 10 DAY FOLLOW-UP COMPARISON

C – REACTIVE PROTEIN	BASELINE		10 DAY		PVALUE FOR COMPARISON OF CRP REDUCTION BETWEEN 3 GROUPS
	MEAN	STDDEV	MEAN	STDDEV	
REGIMEN A	51.78	25.47	9.31	2.28	
REGIMEN B	59.71	23.37	9.27	2.29	
REGIMEN C	51.64	25.13	9.51	2.28	>0.0001

Initial levels of CRP were found to be highest in Regimen B (59.71 mg/L) and were followed by Regimen A (51.78 mg/L) and Regimen C (51.64 mg/L). After 10 days, CRP levels reduced to around 9mg/L in all groups. There is no statistical significance in the reduction between 3 groups with a p-value of > 0.0001 , which means that all regimens are equally effective in reducing the levels of CRP and thus indicated that all the regimens managed the CAP equally, showing effectiveness in the reduction of CRP.

PROCALCITONIN: BASELINE AND 10 DAY FOLLOW-UP COMPARISON

PROCALCITONIN	BASELINE		10 DAY		PVALUE FOR COMPARISON OF PROCALCITONIN REDUCTION BETWEEN 3 GROUPS
	MEAN	STDDEV	MEAN	STDDEV	
REGIMEN A	5.3	2.8	0.3	0.3	
REGIMEN B	5.1	2.7	0.3	0.2	
REGIMEN C	5.0	3.0	0.3	0.2	>0.0001

Initial levels of Procalcitonin were found to be highest in Regimen B (59.71 mg/L) and were followed by Regimen A (5.3 ng/mL), followed by Regimen B (5.1 ng/mL) and Regimen C (5.0 ng/mL). After 10 days, CRP levels reduced to around 0.3 ng/mL in all groups. There is no statistical significance in the reduction between 3 groups with a p-value of > 0.0001 , which means that all regimens are equally effective in reducing the levels of Procalcitonin and thus indicated that all the regimens managed the CAP equally, showing effectiveness in the reduction of Procalcitonin values.

WHITE BLOOD CELLS (WBC): BASELINE AND 10 DAY FOLLOW-UP COMPARISON

WHITE BLOOD CELLS (WBC)	BASELINE		10 DAY		PVALUE FOR COMPARISON OF WBC REDUCTION BETWEEN 3 GROUPS >0.0001
	MEAN	STDDEV	MEAN	STDDEV	
REGIMEN A	10256.78	3371.06	6198.6	3388.8	
REGIMEN B	10565.38	3112.60	6382.7	3241.7	
REGIMEN C	10880.11	3042.33	5842.6	2655.7	

WBC at baseline were significantly elevated due to infection with the highest count in Regimen C (10,880.11 cells/ μ L). After ten days, all regimens were found to decrease WBC counts to normal levels (~6,000 cells/ μ L). There is no statistical significance in the reduction between 3 groups with a p-value of > 0.0001, which means that all regimens are equally effective in infection control.

VITAL SIGNS : BASELINE AND 24hr COMPARISON

VITAL SIGNS	REGIMEN: A			REGIMEN: B			REGIMEN: C		
	BASE LINE	24hr	% CHANGE	BASE LINE	24hr	% CHANGE	BASE LINE	24hr	% CHANGE
Heart Rate Normal (YES)	22	50	-127.3	31	50	-61.3	32	50	-56.3
Respiratory Rate Normal (YES)	32	50	-56.3	22	50	-127.3	28	50	-78.6
Blood Pressure Normal (YES)	21	50	-138.1	23	50	-117.4	23	50	-117.4
Oxygenation Normal (YES)	31	50	-61.3	29	50	-72.4	30	50	-66.7

This table evaluates early normality of vital parameters (heart rate, respiratory rate, blood pressure, oxygenation) 24 hours after commencing the therapeutic regimens. All regimens demonstrate rapid improvements. All 50 patients inside each group achieved heart rate normalization by 24 hours following regimen initiation, with the greatest percentage change in Regimen A (127.3%). Respiratory improvement was most notable under Regimen B (127.3%). This particular finding shows early stabilization in physiologic parameters, particularly with Regimen B.

CLINICAL STABILITY ASSESSMENT

CLINICAL STABILITY	REGIMEN: A	REGIMEN: B	REGIMEN: C	P VALUE
YES	50	50	50	>0.00001
% CLINICAL STABILITY	100%	100%	100%	

The table shows the clinical stability results for three antibiotic regimens used in treatment of community-acquired pneumonia (CAP). After 24hrs of treatment, clinical stability had been attained by 150 patients (100%), and all three regimens showed 100% efficacy in this regard, namely A, B, and C. The p-value is >0.00001 , indicating no statistical difference between any of the groups, thus confirming that all regimens enjoyed equal treatment success in achieving clinical stability in patients having CAP.

TIME TO CLINICAL IMPROVEMENT (DAYS)

TIME TO CLINICAL IMPROVEMENT (DAYS)	REGIMEN: A	REGIMEN: B	REGIMEN: C
Time to Fever Reduction (Days)	4.5	3.82	3.54
Time to Cough Improvement (Days)	4.4	4.22	4.28
Time to Dyspnea Reduction (Days)	5.98	7.08	7.3
Time to X-ray Normalization (Days)	9.5	9.56	9.78
Time to SpO ₂ Normalization (Days)	5.8	5.92	5.9

The table depicting time to clinical improvement in patients of community-acquired pneumonia (CAP) with three different antibiotic regimens showed that fever resolution occurred quickly with Regimen C (3.54 days), while dyspnea resolution was performed quicker with Regimen A (5.98 days). Cough and SpO₂ normalizations appeared to follow similar time frames for all Regimens, around 4.2 and 5.9 days on average. X-ray normalizations took the longest time, on the order of around 9.5–9.78 days. In brief, all regimens are effective in the attainment of clinical improvements.

LENGTH OF HOSPITAL STAY

TIME TO CLINICAL IMPROVEMENT (DAYS)	REGIMEN: A	REGIMEN: B	REGIMEN: C
MEAN	7.62	7.36	7
STD DEV	2.1	2.0	2.0
P VALUE	>0.00001		

The duration of hospital stay for community-acquired pneumonia (CAP) patients across the three antibiotic regimens is detailed in the table. The average hospital stay was 7.62 days for Regimen A, 7.36 days for Regimen B, and 7 days for Regimen C, with standard deviations approximately 2 days across groups. With a p-value of more than 0.00001 as stated, there is no statistically significant difference in the duration of hospital stay indicating that all three regimens were equally effective in reducing hospital stay duration.

MORTALITY

MORTALITY	REGIMEN: A	REGIMEN: B	REGIMEN: C
NO	50	50	50

The table gives mortality outcomes for community-acquired pneumonia (CAP) patients on three antibiotic regimens. All 150 patients (100%) survived; there was no mortality for regimens A, B, and C. This indicates that all treatment regimens were equally effective in preventing mortality, ensuring positive clinical outcomes to all patient groups.

SIDE EFFECTS

SIDE EFFECTS	REGIMEN: A	REGIMEN: B	REGIMEN: C
Diarrhea	7	16	21
Nausea	20	11	8
Rash	10	14	9

Regimen C recorded the highest number of 21 cases of diarrhea, followed by Regimen B with 16 cases and Regimen A with 7 cases for diarrhea. Nausea occurred most often in Regimen A, 20 cases, then Regimen B, 11 cases, and lastly, Regimen C, 8 cases. Rashes were noted in 14 patients (Regimen B), 10 patients (Regimen A), and 9 patients (Regimen C). Side effects differed across regimens; however, they were mostly mild and manageable.

READMISSION AFTER 30 DAYS

READMISSION AFTER 30 DAYS	REGIMEN: A	REGIMEN: B	REGIMEN: C
YES	9	9	6

The table shows the 30-day readmission rates due to community-acquired pneumonia (CAP) across three regimens of antibiotic therapy. Both regimen A and regimen B recorded 9 readmissions each while regimen C had 6 readmissions. Patients were readmitted having mild symptoms, not due to severe complications. Though regimen C seemed to have a little lesser readmission rate, the overall differences were insignificant and, therefore, it could be said that all three regimens were equally effective towards a serious recurrence.

2. DISCUSSION

The study population consisted of 150, patients were evenly distributed across three antibiotic regimens (A, B, and C), each comprising 33.33%, ensuring balanced treatment comparison. Males (52.67%) are larger than females (47.33%). The mean age of the 150 patients studied was 55 years, with the highest percentage of patients in the range of 51-60 years (22.67%). Those living in the urban area were slightly more (51.33%) than those in the rural area (48.67%). A smoking history was significant, with 41.33% being ex-smokers and 34% being current smokers. Alcohol use was reported at 53.33%. The most common comorbidity was hypertension (30.85%), followed by diabetes (25.53%) and heart ailments (24.47%). 51.33% had a family history of CAP, indicating genetic or environmental susceptibility, emphasizing the need for preventive strategies in high-risk individuals.

The sputum culture showed *Streptococcus pneumoniae* as the pathogen most frequently isolated in 67 patients (44.67%). *Haemophilus influenzae* was the second most common, in 55 patients (36.67%), while *Klebsiella pneumoniae* was present in 28 patients (18.67%). These findings confirm that *S. pneumoniae* is still the major causative agent for respiratory infections in the given population, as also indicated in other parts of the world.

The evaluation of clinical improvement in patients suffering from pneumonia with a community acquired pneumonia (CAP) using three treatment regimens gave the results that regimen C of treatment had the greatest improvement percentage rates, followed by regimen B, and regimen A. The highest rate of resolution of fever (76.0%) was observed with regimen C; this was followed by regimen B (65.2%) and regimen A (53.8%). Cough improvement was at 65.2% for regimen C, 58.8% for regimen B, and 58.3% for regimen A. The biggest drop in dyspnea was noted in regimen C (77.3%); next was regimen B (66.7%), followed by regimen A (53.6%). Of the abnormal X-ray findings, 83.9% patients' findings resolved in regimen C, 72.0% in regimen B, and 69.0% in regimen A. The highest for normalization of SpO₂ was also for regimen C (70.0%). Clinical improvement was observed for all of the regimens; however, maximum improvement was noted in Regimen C (84.00%); next was Regimen B (72.00%) and finally Regimen A (64.00%). There is no significant difference among improvements among the three regimes (χ^2 test, $p > 0.00001$) mean that all three regimes have shown an equal clinical improvement, but definitely Regimen C performed much better than the other two and is likely to be the best treatment of the three regimens studied.

The study showed that the three treatments proved equally effective in decreasing the inflammatory and infection markers in a community-acquired pneumonia (CAP) patient. Level of CRP, procalcitonin, and WBC markedly reduced after 10 days

of treatment, there was no statistical difference in the measurement among the groups ($p > 0.0001$). Reduction in CRP was from about 50-60 mg/L to about 9 mg/L; Procalcitonin reduced from about 5 ng/mL to about 0.3 ng/mL, while WBC decreased from about 10,000 cells/ μ L to about 6,000 cells/ μ L. These findings proved that the results achieved by all regimens were almost the same infection control and inflammatory reduction. It indicates that they are equally effective in CAP management.

A comparison of vital signs before and after 24 hours of therapy for community-acquired pneumonia (CAP) revealed considerable improvement in all three antibiotic regimens. Heart and respiratory rates, blood pressure, and oxygenation normalized in all groups, reflecting rapid stabilization. Thus, clinical stability was achieved in 100% of patients across all regimens, with no statistically significant difference among them ($p > 0.00001$). This reveals that each of the three regimens was equally effective both in vital functions restoration and early clinical stability. These findings indicate that any of the regimens could be reliably employed for management of the patient with CAP, as treatment success was found comparable across the three regimens.

The time to clinical improvement after three antibiotic regimens for community-acquired pneumonia (CAP) varied as follows: fever resolution was quickest with Regimen C (3.54 days), whereas Regimen A earlier improved dyspnea (5.98 days); cough resolution and SpO₂ normalization were achieved with similar timing between the regimens, approximately 4.2 and 5.9 days, respectively; longest was X-ray normalization (~9.5–9.78 days); and length of hospital stay was comparable across regimens without significant difference ($p > 0.00001$). The above conditions therefore point at all three regimens similarly achieving clinical improvement and hence reducing the hospitalization duration.

All the 150 patients survived, indicating that the three antibiotic regimens were equally effective in preventing mortality in community-acquired pneumonia (CAP). However, the side effects associated with each regimen were different whereby most common was diarrhea in Regimen C (21 cases), nausea in Regimen A (20 cases), and rash in Regimen B (14 cases), but all were mild and manageable. The readmission rates within thirty days were almost the same across regimens with 9 cases each for Regimens A and B and 6 for Regimen C. Although Regimen C had fewer readmissions, the difference was not statistically significant, confirming comparable efficacies across all three regimens.

3. CONCLUSION

Community-acquired pneumonia treatments analyzed revealed that all the three antibiotic regimens yielded a significant improvement in clinical status, normalization of vital signs, and substantial declines in inflammatory markers as well as radiologic abnormalities by day 10. Clinical improvement was observed in the majority of patients across all groups: 64% in Regimen A; 72% in Regimen B; and 84% in Regimen C. All regimens also provided 100% clinical stability and were associated with no mortality, thus indicating that all the regimens performed well in terms of efficacy and safety. Although Regimen C seemed to relieve symptoms a bit faster with a lower readmission rate, all three regimens can be considered clinically effective treatment options. Findings thus favor antibiotic utilization in patients with any of the regimens tested. When choosing regimens, however, patient-specific factors and tolerability should guide the decision. Further multicentric trials may help optimize the therapeutic strategy.

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