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# Emergency Department Use of Intravenous Procainamide for Patients with Acute Atrial Fibrillation or Flutter

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## Abstract

**Objectives:** Acute atrial fibrillation and flutter are very common arrhythmias seen in emergency department (ED) patients, but there is no consensus for their optimal management. The objective of this study was to examine the efficacy and safety of intravenous (IV) procainamide for acute atrial fibrillation or flutter.

**Methods:** This health records review included a consecutive cohort of ED patients with acute-onset atrial fibrillation or atrial flutter who received IV procainamide at one university hospital ED during a five-year period. The standard clinical protocol involved IV infusion of 1 g of procainamide over 60 minutes, followed by electrical cardioversion if necessary. A trained observer extracted data from the original clinical records. Outcome measurements included conversion to sinus rhythm, adverse events, and relapse up to seven days.

**Results:** The 341 study patients had a mean age of 63.9 years (SD  $\pm$  15.5 years), and 56.6% were male. The conversion rates were 52.2% (95% confidence interval = 47% to 58%) for 316 atrial fibrillation cases and 28.0% (95% confidence interval = 13% to 46%) for 25 atrial flutter cases. Mean dose given was 860.7 mg (SD  $\pm$  231.2 mg), and median time to conversion was 55 minutes. Adverse events occurred in 34 cases (10.0%): hypotension, 8.5%; bradycardia, 0.6%; atrioventricular block, 0.6%; and ventricular tachycardia, 0.3%. There were no cases of torsades de pointes, cerebrovascular accident, or death. Most patients (94.4%) were discharged home, but 2.9% of patients returned with a recurrence of atrial fibrillation within seven days.

**Conclusions:** This study of acute atrial fibrillation or flutter patients treated in the ED with IV procainamide suggests that this treatment is safe and effective in this setting. Procainamide should be prospectively compared with other ED strategies.

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**Keywords:** atrial fibrillation, procainamide

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Atrial fibrillation is the most common form of acute arrhythmia in patients who present to the emergency department (ED).<sup>1</sup> Atrial fibrillation is defined as a cardiac arrhythmia characterized by disorganized atrial electrical depolarization leading to an irregular and often rapid ventricular rate. Emergency physicians often manage patients with either acute or

chronic atrial fibrillation. For patients with “chronic” or “permanent” atrial fibrillation, cardioversion has previously failed or clinical judgment has led to a decision not to pursue cardioversion.<sup>2</sup> Such patients occasionally require rate control in the ED. Patients are considered to have “acute,” “paroxysmal,” or “new-onset” atrial fibrillation if the onset is very recent and/or cardioversion remains a treatment option. Management for these patients is much more complex and controversial and constitutes the focus of this article. The frequency of acute atrial fibrillation as a presenting complaint in the ED is not well documented. Michael et al. identified 289 patients with acute atrial fibrillation in a database search over 18 months at a tertiary care hospital ED that had 60,000 visits annually, representing 0.5% of all emergency visits.<sup>3</sup> Atrial flutter is less commonly seen but is a significant therapeutic challenge in the ED. This arrhythmia is characterized by rapid, regular, atrial

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depolarizations at a characteristic rate of approximately 300 beats/min and presents with varying degrees of atrioventricular block. Atrial flutter is less common than atrial fibrillation and often requires urgent electrical cardioversion.

There is no universally accepted consensus for the optimal strategy to treat patients with acute atrial fibrillation or flutter.<sup>4-6</sup> In the ED, controversy exists surrounding the issue of conservative (rate control) versus aggressive (rhythm control) treatment. Conservative treatment has consisted of rate control, anticoagulation, and possibly delayed cardioversion, whereas with aggressive treatment, the patient is cardioverted to sinus rhythm in the ED, either pharmacologically or electrically.<sup>7-9</sup> Most studies comparing conservative with aggressive management strategies deal with patients in chronic atrial fibrillation, and their findings do not directly apply to acute atrial fibrillation.<sup>10</sup>

There is little discussion in the literature to encourage the use of intravenous (IV) procainamide for treatment of patients with acute atrial fibrillation or flutter. Recommendations from the 2006 American College of Cardiology/American Heart Association/European Society of Cardiology guidelines refer to amiodarone, dofetilide, flecainide, ibutilide, and propafenone as being proven effective for pharmacologic conversion of atrial fibrillation and list procainamide as a "less effective or incompletely studied agent."<sup>5</sup> Procainamide is mentioned only briefly in the Canadian Journal of Cardiology guidelines.<sup>11</sup> In our institution, emergency physicians routinely use IV procainamide to attempt cardioversion of atrial fibrillation.<sup>3</sup> To our knowledge, no other centers worldwide have reported using IV procainamide frequently. The objectives of the current study were to examine the efficacy and safety of IV procainamide for acute atrial fibrillation and flutter. Specifically, we sought to review the effectiveness of emergency cardioversion and the frequency of adverse events.

## METHODS

### Study Design

This was a retrospective study of ED health records of patients presenting with acute atrial fibrillation or flutter. The hospital research ethics board approved the protocol without the need for informed consent.

### Study Setting and Population

The study was conducted at the Ottawa Hospital Civic Campus ED and included individual patients seen during the 5½-year period from January 1, 2000, to June 30, 2005, inclusive. The Ottawa Hospital is an adult, tertiary care institution affiliated with the University of Ottawa, and the Civic Campus has an annual ED census of 60,000 visits. We included a consecutive cohort of individual ED patients presenting with the primary diagnosis of acute atrial fibrillation or atrial flutter and who received IV procainamide. For patients with more than one ED visit during the study period, we only included the first presentation. We excluded patients with chronic atrial fibrillation (permanent or long-standing), patients with symptoms for more than 48 hours unless currently anticoagulated, patients with another diagnosis necessi-

tating admission (e.g., cardiac ischemia or congestive heart failure), and those with unknown duration of symptoms. We did not exclude patients whose treatment for atrial fibrillation in the ED resulted in a complication necessitating admission.

### Study Protocol

The following describes the clinical protocol that is considered "routine care" for patients with acute atrial fibrillation in our institution. The attending staff emergency physicians make the decision to attempt rhythm or rate control, but the former is considered routine care for most patients. This usually includes an attempt to cardiovert chemically with IV procainamide, followed by electrical cardioversion if necessary. There is no upper age limit to rhythm control. Every effort is made to clarify that the time of onset is less than 48 hours, and if this cannot be verified, then rate control is pursued unless the patient is on warfarin and has a therapeutic international normalized ratio. Rhythm control with procainamide is generally not given if the patient is unstable with cardiac ischemia, severe congestive heart failure, or hypotension. In addition, procainamide is not given if records indicate the patient had resistance to this medication on previous visits. Patients are not routinely screened for elevation of cardiac enzyme levels unless there is chest pain or ST-T wave changes.

Administration of procainamide generally commences within one hour of the patient's arrival to the hospital. The standard protocol in our ED is to give 1 g of procainamide in 250 mL of dextrose and water as a controlled infusion over one hour, under constant cardiac and blood pressure monitoring. The infusion is interrupted if blood pressure falls to <100 mm Hg; if a bolus of 250 mL of normal saline corrects the blood pressure, the infusion is resumed. The infusion is discontinued if the patient's rhythm converts to sinus rhythm, if hypotension persists, or if bradyarrhythmia occurs. Hence, for patients whose rhythm converts, <1 g is given.

If chemical cardioversion fails, most patients then undergo electrical cardioversion. Those patients who are cardioverted by procainamide typically spend about four hours in the ED. Those who require electrical cardioversion typically are discharged within eight hours of arrival. Patients who are successfully cardioverted are usually discharged without medication, that is, no oral anticoagulants, rate control agents, or rhythm control agents. Outpatient cardiology follow-up is usually recommended. Patients who are not cardioverted in the ED have their rate controlled and are then discharged on oral anticoagulants and rate control medication.

Patients were identified from the Ottawa Hospital health records database, which uses the Canadian National Ambulatory Care Reporting System, designed to capture data on patients visiting Canadian EDs. Identification was based on the main diagnosis of atrial fibrillation or atrial flutter, combined with a procedure code of antiarrhythmic IV therapy. A single trained research nurse, blinded to the study objectives, reviewed the original patient charts of all cases to determine patient eligibility and then abstracted study data. Before abstraction of patient information, the study variables were explicitly defined, and a standardized data collection form was

used. The 30 variables included demographic characteristics, clinical descriptors, medical interventions, adverse events, and return visits to the ED. The study data were entered into an electronic database. Selected cases were also reviewed by the principal author. Cases with missing data for specific variables were deleted from the denominator for the descriptive analyses for those variables.

### Outcome Measures

The primary outcomes were rate of conversion to sinus rhythm, defined as a return to sinus rhythm before discharge from the ED, and the determination of adverse events. Adverse events included the following within six hours of IV procainamide administration: hypotension, defined as a systolic blood pressure <100 mm Hg during infusion; bradycardia, defined as a heart rate <60 beats/min during infusion; syncope; second or third degree heart block; ventricular tachyarrhythmia; atrial tachyarrhythmia; torsades de pointes; cerebrovascular accident; and death. Additional measurements included time to conversion, average dose of IV procainamide required, QTc prolongation, and admission to the hospital. We selected a random sample of 50 charts to review lengths of stay in the ED, from registration to discharge. We also monitored records for evidence, within seven days, of death, cerebrovascular accident, and relapse to atrial fibrillation. Adverse events and other outcomes were ascertained from review of the ED record (physician and nursing progress notes, electrocardiogram readings, consultations), hospital computerized records, and quality assurance reviews. If not mentioned, we assumed these adverse events did not occur. Many patients, if stable, were discharged in less than six hours posttreatment. The Ottawa Hospital sees two thirds of all adult ED visits for the region and is the sole regional cardiology referral center.

### Data Analysis

We calculated descriptive statistics using proportions or means with standard deviations, as appropriate for the data. We used SAS software (SAS Institute, Inc., Cary, NC) version 9.1 TS Level 1M3 for data entry and the descriptive statistics.

## RESULTS

From January 2000 to June 2005, there were 1,057 ED patient visits with a primary diagnosis of acute atrial fibrillation or flutter, and among these were 660 visits where IV procainamide was administered. After excluding repeat visits, we identified 341 individual patients whose first visits were included in this study. Of these study patients, 31.4% (107) had a total of 319 repeat visits excluded from this study (ranging from 50 patients with two visits for acute atrial fibrillation during the study period to two patients who had 16 visits each).

Table 1 summarizes the characteristics of the 341 study patients, including 316 with acute atrial fibrillation and 25 with acute atrial flutter. The mean patient age was 63.9 years (range, 19–92; SD  $\pm$  15.5 years), 56.6% were men, and the mean duration of arrhythmia before presentation was 8.2 hours (SD  $\pm$  11.9 hours).

Treatments given are shown in Table 2, with 100% of cases receiving IV procainamide and 144 (42.2%) subse-

quently undergoing electrical cardioversion with a success rate of 91.0%. Of all included patients, 94.4% were discharged home from the ED and 88.9% were discharged home in sinus rhythm. A random sample of 50 charts found that those patients converted by procainamide ( $n = 25$ ) spent an average of 4.4 hours in the ED before discharge (range, 2–8.5 hours), and those converted electrically ( $n = 25$ ) spent an average of 7.4 hours in the ED (range, 3.5–16 hours).

Table 3 describes the ED use of IV procainamide and shows an overall successful conversion with procainamide of 172 patients (50.4%). The conversion rates were 52.2% (95% confidence interval [CI] = 47% to 58%) for the atrial fibrillation cases and 28.0% (95% CI = 13% to 46%) for the atrial flutter cases. The mean dose of IV procainamide given was 860.7 mg (SD  $\pm$  231.2 mg) for all cases, and the median time to conversion was 55 (range, 2–390) minutes.

Adverse events occurred in 10.0% (95% CI = 7% to 13%) of patients overall, with 9.8% in those with atrial fibrillation and 12.0% in those with atrial flutter (Table 4). Hypotension during infusion was the most common adverse event, occurring in 29 patients (8.5%; 95% CI = 6% to 12%), and most of these events were very transient. No patients experienced syncope, torsades de pointes, myocardial infarction, cerebrovascular accident, or death. In addition, only 19 patients (5.6%) were admitted, and 10 (2.9%) were discharged from the ED and later returned to our institution with a relapse of atrial fibrillation within seven days.

## DISCUSSION

To our knowledge, this is the largest reported review of ED patients with acute atrial fibrillation or flutter treated with IV procainamide. We found, in our setting, that procainamide appears to be a safe and effective treatment for acute atrial fibrillation but less so for atrial flutter. Our results indicate that IV procainamide was effective in converting 52.2% of patients with acute atrial fibrillation but only 28.0% with atrial flutter. The median time to conversion was 55 minutes, and lengths of stay in the ED were relatively brief for those who were converted to normal sinus rhythm. In addition, IV procainamide is safe with few significant adverse events documented. Only 10% of patients experienced an adverse event, with transient hypotension being the most common. Moreover, only ten patients returned to our institution with a relapse of atrial fibrillation within seven days. We believe that these data support the use of IV procainamide for early pharmacologic cardioversion of acute atrial fibrillation in the ED.

Very few studies have previously evaluated procainamide in the ED for acute atrial fibrillation. Michael et al. reviewed 180 patients with acute atrial fibrillation (<48 hours) who underwent attempted conversion with procainamide, with a 50% success rate and a 5% rate of hypotension.<sup>3</sup> In a randomized comparison with flecainide, Madrid et al. found that procainamide had a 65% conversion rate for 40 patients in acute atrial fibrillation of duration less than 24 hours.<sup>12</sup> Two small studies from the early 1980s by Halpern et al. ( $N = 20$ ) and Fenster et al. ( $N = 26$ ) found conversion rates of 43% and 58%,

Table 1  
Baseline Characteristics for 341 Individual Patients Presenting with Atrial Fibrillation and Atrial Flutter

	All Patients (N = 341)	Atrial Fibrillation (n = 316)	Atrial Flutter (n = 25)
Age, median (yr)	68	68	63
Range	19–92	19–92	32–87
Male (%)	193 (56.6)	178 (56.3)	15 (60.0)
Duration of arrhythmia, mean (hr)	8.2	8.3	6.2
Range	0.1–96	0.1–96	0.3–24
Main presenting symptom (%)			
Palpitations	253 (74.2)	236 (74.7)	17 (68.0)
Chest pain	46 (13.5)	44 (13.9)	2 (8.0)
Shortness of breath	18 (5.3)	14 (4.4)	4 (16.0)
Dizziness	9 (2.6)	9 (2.9)	0 (0.0)
Syncope	5 (1.5)	5 (1.6)	0 (0.0)
Other	10 (2.9)	8 (2.5)	2 (8.0)
Medical history (%)			
Previous atrial fibrillation	223 (65.4)	214 (67.7)	9 (36.0)
Hypertension	112 (32.8)	104 (32.9)	8 (32.0)
Coronary artery disease	85 (24.9)	73 (23.1)	12 (48.0)
Thyroid disease	41 (12.0)	38 (12.0)	3 (12.0)
Valvular heart disease	18 (5.3)	13 (4.1)	5 (20.0)
Congestive heart failure	18 (5.3)	16 (5.1)	2 (8.0)
Thromboembolic disease	17 (5.0)	14 (4.4)	3 (12.0)
Chronic lung disease	16 (4.7)	15 (4.8)	1 (4.0)
Home medications (%)			
$\beta$ -blockers	115 (33.7)	103 (32.6)	12 (48.0)
Warfarin	68 (19.9)	62 (19.6)	6 (24.0)
Calcium channel blockers	52 (15.3)	50 (15.8)	2 (8.0)
Sotalol	29 (8.5)	29 (9.2)	0 (0.0)
Digoxin	23 (6.7)	21 (6.7)	2 (8.0)
Amiodarone	9 (2.6)	9 (2.9)	0 (0.0)
Procainamide	2 (0.6)	2 (0.6)	0 (0.0)
Heart rate on arrival (beats/min)	122.7	122	131.7
Oxygen saturation on arrival (mean %)	97.7	97.7	97.4
Systolic blood pressure, mean (mm Hg)	134.7	135.2	128.9
Previous successful cardioversion (%)	119 (34.9)	113 (35.8)	6 (24.0)
Electrical	53 (15.5)	49 (15.5)	4 (16.0)
Procainamide	46 (13.5)	45 (14.2)	1 (4.0)

respectively, with procainamide.<sup>13,14</sup> Two other studies by Volgman et al. and Stambler et al. found much lower conversion rates with procainamide, likely because most patients had been in atrial fibrillation for longer periods, up to 90 days.<sup>15,16</sup>

Several other drugs can be considered for the pharmacologic cardioversion of atrial fibrillation in the ED.<sup>6–8,17,18</sup> According to the American College of Cardiology/American Heart Association/European Society of Cardiology practice guidelines, the following are classes of

Table 2  
ED Treatment for 341 Individual Patients Presenting with Atrial Fibrillation and Atrial Flutter

	All Visits (N = 341)	Atrial Fibrillation (n = 316)	Atrial Flutter (n = 25)
IV rate control drugs in ED (%)	169 (49.6)	157 (49.7)	12 (48.0)
Metoprolol	108 (31.7)	101 (32.0)	7 (28.0)
Diltiazem	67 (19.7)	63 (19.9)	6 (18.8)
Digoxin	4 (1.2)	4 (1.3)	0 (0.0)
Verapamil	3 (0.9)	2 (0.6)	1 (4.0)
IV chemical cardioversion attempted (%)*	341 (100)	316 (100)	25 (100)
Successful if attempted	172 (50.4)	165 (52.2)	7 (28.0)
Subsequent electrical cardioversion (%)			
Attempted	144 (42.2)	129 (40.8)	15 (60.0)
Successful if attempted (n = 144, n = 129, and n = 15, respectively)	131 (91.0)	116 (89.9)	15 (100)
Maximum energy used (joules)	360	360	200
Total number of shocks given, median (%)	1	1	1
Range	1–5	1–5	1–2
Discharged home (%)	322 (94.4)	299 (94.6)	23 (92.0)
Discharged home in sinus rhythm (%)	303 (88.9)	281 (88.9)	22 (88.0)

\* All chemical cardioversion attempts made with IV procainamide.

**Table 3**  
ED Treatment with Procainamide for 341 Individual Patients Presenting with Atrial Fibrillation and Atrial Flutter

	All Visits (N = 341)	Atrial Fibrillation (n = 316)	Atrial Flutter (n = 25)
Conversion with procainamide (%)	172 (50.4)	165 (52.2)	7 (28.0)
Procainamide dose, mean (mg)	860.7	863.9	820
Range	250–1,500	250–1,500	500–1,000
Time to conversion, median (min)	55	55	35
Range	2–390	2–390	15–145
Heart rate, mean (beats/min)			
Preconversion	128.9	127.9	140.9
Postconversion	71.7	71.2	79
ECG QTc interval, mean (ms)			
Preconversion	406.1	405.9	408.9
Postconversion	428.7	428	437.4

recommendation for oral or IV agents for atrial fibrillation of less than seven days' duration: class I, proven efficacy (dofetilide, flecainide, ibutilide, propafenone); class IIa, proven efficacy (amiodarone); class IIb, less effective (disopyramide, procainamide, quinidine); and class III, should not be used (digoxin, sotalol).<sup>5</sup> The quality of evidence, particularly for acute atrial fibrillation of less than 48 hours' duration, is often weak, and some agents are only available in Europe. There is a need for larger clinical trials conducted in the ED comparing these agents in patients with acute fibrillation.

The use of dofetilide has been restricted in the United States by the Food and Drug Administration due to the risk of torsades de pointes. Flecainide has not gained widespread use, likely due to the common occurrence of arrhythmias following administration.<sup>19–21</sup> IV ibutilide is a widely used agent with effectiveness for both atrial fibrillation and flutter.<sup>15,22–27</sup> Ibutilide has a 4% incidence of torsades de pointes, and serum potassium and magnesium levels should be measured before use. Propafenone can be used orally or intravenously and appears to be effective in 56%–83% of cases, although the IV formulation is not available in the United States.<sup>21,28</sup> The effectiveness of amiodarone for acute atrial fibrillation is not clear, with some meta-analyses suggesting it is no more effective than placebo or is associated with adverse reactions.<sup>29–34</sup> Recently, a randomized controlled trial of vernakalant (RSD1235), a novel, atrial-selective, antiarrhythmic agent currently approved for investigational use only, demonstrated high clinical efficacy: 61% for conversion of recent-onset atrial fibrillation.<sup>35</sup>

Our study suggests that treatment with IV procainamide is a reasonable alternative for the pharmacologic cardioversion of patients with acute atrial fibrillation, because conversion was achieved more than 50% of the time. Moreover, this therapy is associated with a very low incidence of serious adverse events and allows patients to be safely discharged from the ED without the need for anticoagulation or subsequent outpatient electrical cardioversion. Furthermore, if procainamide

**Table 4**  
Adverse Events and Other Outcomes for 341 Study Patients

	All Visits (N = 341)	Atrial Fibrillation (n = 316)	Atrial Flutter (n = 25)
Adverse events (%)	34 (10.0)	31 (9.8)	3 (12.0)
Hypotension (systolic blood pressure <100 mm Hg)	29 (8.5)	27 (8.5)	2 (8.0)
Bradycardia (heart rate <60 beats/min)	2 (0.6)	2 (0.6)	0 (0.0)
Atrioventricular block	2 (0.6)	2 (0.6)	0 (0.0)
Atrial tachyarrhythmia	2 (0.6)	2 (0.6)	0 (0.0)
Ventricular tachyarrhythmia	1 (0.3)	1 (0.3)	0 (0.0)
Syncope	0 (0.0)	0 (0.0)	0 (0.0)
Torsades de pointes	0 (0.0)	0 (0.0)	0 (0.0)
Myocardial infarction	0 (0.0)	0 (0.0)	0 (0.0)
Cerebrovascular accident	0 (0.0)	0 (0.0)	0 (0.0)
Death	0 (0.0)	0 (0.0)	0 (0.0)
Admitted	19 (5.6)	17 (5.4)	2 (8.0)
Relapse within seven days	10 (2.9)	9 (2.9)	1 (4.0)

fails to convert the patient, it does not prevent the use of immediate electrical cardioversion. There are substantial advantages to this approach, such as avoiding unnecessary hospital admissions, lengthy ED stays, or the need for patients to be in an unpleasant and debilitating rhythm for up to four weeks while awaiting elective outpatient cardioversion. Once cardioverted in the ED, our patients are able to immediately resume a normal lifestyle, including return to work or sports activities.

Our study also strongly suggests that randomized trials comparing IV procainamide with other drug regimens for treatment of acute atrial fibrillation should be conducted with antiarrhythmic agents such as ibutilide, propafenone, or vernakalant (RSD1235).

## LIMITATIONS

The study was not conducted prospectively but was a retrospective health records review, which can have problems with missed cases, incomplete charting, and review bias. Nevertheless, we are confident that we captured all possible eligible cases by querying the Canadian National Ambulatory Care Reporting System database and performing a detailed review by a well-trained study nurse. This was a consecutive and comprehensive cohort of individual ED patients. The review process had full access to physician's notes, nursing progress notes, and inpatient records, and it is unlikely that a significant ED adverse event would have been overlooked.

We cannot be fully confident that all adverse events after ED discharge were identified because we did not attempt telephone follow-up or death registry review. Nevertheless, we believe that significant missed outcomes are very unlikely, because the study institution is the sole regional cardiology referral center in this mid-sized city.

This observational study had no control group that might have permitted comparison with placebo or other drugs such as ibutilide. Nevertheless, the data provide

reasonably precise estimates of effectiveness and safety for the use of IV procainamide. The study was conducted at one hospital only and included relatively few atrial flutter cases ( $n = 25$ ). Nevertheless, we did collect a large series of cases and believe our results are applicable to most EDs. We recognize that the study population represents a select group of patients for whom the treating physician elected to use procainamide, and we did not attempt to characterize the reason for this choice of treatment. In an attempt to reduce selection bias, we only included individual patients once in this study, even though some patients had many episodes of procainamide treatment during the study period.

## CONCLUSIONS

Pharmacologic cardioversion with IV procainamide in our setting appears to be safe and effective in the ED treatment of acute atrial fibrillation but less effective for acute atrial flutter. Acute conversion in the ED obviates the need for anticoagulation and follow-up visits for elective electrical cardioversion. This approach has the potential to save both patient time and health care resources. Future randomized trials should compare IV procainamide with other drug regimens.

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