Patient Reported Outcomes from ATLAS-2M

Summary

- Long-acting cabotegravir and rilpivirine (CAB + RPV LA) provided high treatment satisfaction and acceptance irrespective of prior CAB + RPV LA exposure at study entry.
- Of those without prior experience of CAB + RPV LA, a large increase in treatment satisfaction and acceptance for long-acting treatment over prior daily oral treatment was observed for both every-8-week and every-4-week dosing schedules.
- For participants transitioning from the every-4-week arm in ATLAS, high treatment satisfaction and acceptance were maintained after more than 96 weeks on CAB + RPV LA therapy.
- Most participants preferred every-8-week and every-4-week dosing over daily oral dosing, with every-8-week dosing also preferred over every-4-week dosing.
- Important Safety Information and Boxed Warning can be found in the Prescribing Information and can also be accessed from the Our HIV Medicines section of viivhealthcare.com/us.

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Patient reported outcomes were assessed in ATLAS-2M utilizing multiple instruments as well one single-item question on participant preference for CAB + RPV LA.[1,2] See Table 1 below.

Table 1. Patient Reported Outcomes Assessments in ATLAS-2M[1]

Instrument	Assessment	Timepoints
Secondary Endpoints (pre-specified)		
HIV Treatment Satisfaction Questionnaire status and change versions (HIVTSQs/c)	Patient satisfaction with HIV treatment	Status version: baseline, W4, W24, W48 Change version: W48
Chronic Treatment Acceptance (ACCEPT) General Acceptance dimension	Patient acceptance of treatment	Baseline, W8, W24, W48
Perception of Injection (PIN) questionnaire	Acceptability and bother of pain and injection-site reactions	W8, W24, W48
HIV/AIDS Targeted Quality of Life (HAT-QoL)	Overall function and wellbeing. Only 3 out of 9 dimensions were assessed.	Baseline, W24, W48
Preference of HIV treatment (single question) and 2 follow-up questions on reasons for preference	Patient preference for CAB + RPV LA (every 4 or 8 weeks) versus oral CAB + RPV, and preference for CAB + RPV LA every 4 weeks versus every 8 weeks	W48

s/c = status and change versions; W = week; CAB + RPV LA = long-acting cabotegravir and rilpivirine

HIVTSQ

Treatment satisfaction was assessed using an adaptation of the validated 10-item HIV Treatment Satisfaction Questionnaire (HIVTSQ), in which two additional items were added to account for changes in HIV treatments, including the recent development of injectable long-acting formulations.[3,4] The new version was found to have better psychometric properties than the old 10-item version and is pending publication.

Status Version (HIVTSQs)

For subjects **without prior exposure** to CAB + RPV LA baseline HIVTSQs mean (standard deviation [SD]) total scores were similar between the two treatment groups at 57.73 (9.21) for the every-8-week group and 56.72 (9.34) for the every-4-week group.[1]

HIVTSQs total scores significantly improved from baseline to Weeks 24 and 48 in both groups, after adjusting for baseline score, sex at birth, age, race, and third-agent class.[1] See Table 2 below.

A statistically significant difference between the every-8-week and every-4-week arms was observed at both timepoints, in favor of every-8-week dosing.

For subjects without prior CAB + RPV exposure, key drivers for change from Baseline in HIVSTQs total score were items 6 (flexibility of recent HIV treatment), 5 (convenience associated with HIV treatment) and 10 (satisfaction to continue with present HIV treatment).

Table 2. Change from Baseline in Total Treatment Satisfaction Score by Visit (ITT-E Population; Without Prior Exposure to CAB + RPV LA) Assessed with HIVTSQs in ATLAS-2M[1]

Visit	Treatment	n	Adjusted Mean (95% CI)*	Adjusted Mean Difference (95% CI)	*P* value
Week 24	Every 8 weeks	319	5.07 (4.36, 5.78)	1.07 (0.07, 2.07)	0.036
	Every 4 weeks	323	4.0 (3.29, 4.70)		
Week 48	Every 8 weeks	319	4.86 (4.02, 5.69)	1.74 (0.56, 2.91)	0.004
	Every 4 weeks	323	3.12 (2.29, 3.95)		

*adjusted for baseline score, sex, age, race, and third-agent class.

ITT-E = intent-to-treat-exposed; CAB + RPV LA = long-acting cabotegravir and rilpivirine; HIVTSQs = HIV Treatment Satisfaction Questionnaire Status Version; CI = confidence interval

HIVTSQs mean (SD) total scores for subjects **with prior exposure** to CAB + RPV LA (≥1 weeks) were high at baseline (62.22 [5.41] points for the every-8-week group and 61.98 [6.72] points for the every-4-week group) and remained stable across Weeks 24 and 48 after adjusting for baseline score, sex at birth (female, male), age (<50, ≥50 years), race (white, non-white) and prior exposure to CAB + RPV (1 to 24, >24 weeks), without significant differences between the two treatment groups.[1] See Table 3 below.

Table 3. Change from Baseline in Total Treatment Satisfaction Score by Visit (ITT-E Population; With Prior Exposure to CAB + RPV LA) Assessed with HIVTSQs in ATLAS-2M[1]

Visit	Treatment	n	Adjusted Mean (95% CI)*	Adjusted Mean Difference (95% CI)	*P* value
Week 24	Every 8 weeks	191	0.59 (-0.03, 1.21)	0.07 (-0.81, 0.95)	0.871
	Every 4 weeks	193	0.52 (-0.10, 1.14)		
Week 48	Every 8 weeks	191	0.44 (-0.27, 1.15)	0.48 (-0.5, 1.48)	0.344
	Every 4 weeks	193	-0.05 (-0.75, 0.66)		

*adjusted for baseline score, sex, age, race, and prior exposure to CAB + RPV LA.

ITT-E = intent-to-treat-exposed; CAB + RPV LA = long-acting cabotegravir and rilpivirine; HIVTSQs = HIV Treatment Satisfaction Questionnaire Status Version; CI = confidence interval

Change Version (HIVTSQc)

HIVTSQc was administered at Week 48 in both groups, to assess satisfaction with CAB+RPV LA and how it compares to the HIV therapy subjects were receiving prior to entering the study, with the intention to account for potentially high baseline values (ceiling effects) with HIVTSQs.[1]

High total HIVTSQc scores were reported in both treatment groups at Week 48 for subjects **without prior exposure** to CAB + RPV LA. The change in satisfaction from prior treatment (oral antiretroviral therapy) significantly favored the every-8-week group compared with every-4-week group at Week 48. See Table 4 below.

Table 4. Change from Baseline in Total Treatment Satisfaction Score by Visit (ITT-E Population; Without Prior Exposure to CAB + RPV LA) Assessed with HIVTSQc in ATLAS-2M[1]

Treatment	n	Adjusted Mean*	Adjusted Mean Difference (95% CI)	*P*-value
Every 8 weeks	312	28.9	1.9 (0.5, 3.2)	0.008
Every 4 weeks	315	27.1		

*adjusted for sex at birth, age, and race.

Note: 12-item HIVTSQc min score: -33 (much less satisfied now); max score: 33 (much more satisfied now).

ITT-E = intent-to-treat-exposed; CAB + RPV LA = long-acting cabotegravir and rilpivirine; HIVTSQc = HIV Treatment Satisfaction Questionnaire Change Version; CI = confidence interval

HIVTSQc scores for subjects **with prior exposure** to CAB + RPV LA in both treatment groups were also high at Week 48.[1] A significant difference favoring the every-8-week group compared with the every-4-week group in change in satisfaction from prior treatment (every-4-week CAB + RPV LA) was reported at Week 48. See Table 5 below.

Table 5. Change from Baseline in Total Treatment Satisfaction Score by Visit (ITT-E Population; With Prior Exposure to CAB + RPV LA) Assessed with HIVTSQc in ATLAS-2M[1]

Treatment	n	Adjusted Mean*	Adjusted Mean Difference (95% CI)	*P*-value
Every 8 weeks	124	29.1	4.4 (2.0, 6.9)	<0.001
Every 4 weeks	125	24.7		

*adjusted for sex at birth, age, and race.

Note: 12-item HIVTSQc min score: -33 (much less satisfied now); max score: 33 (much more satisfied now).

ITT-E = intent-to-treat-exposed; CAB + RPV LA = long-acting cabotegravir and rilpivirine; HIVTSQc = HIV Treatment Satisfaction Questionnaire Change Version; CI = confidence interval

ACCEPT

The ACCEPT questionnaire is a generic medication acceptance measure validated for chronic conditions to assess how participants weigh advantages and disadvantages of long-term medications.[5] While the ACCEPT questionnaire consists of 25 items that capture six dimensions, only the three questions that focus on General Acceptance of study medication were used in this study.

For subjects **without prior exposure** to CAB + RPV LA, mean (SD) Baseline General Acceptance scores were similar between the two treatment groups at 81.5 (25.23) points for the every-8-week group and 81.8 (25.98) points for the every-4-week group, out of a maximum of 100 points (0=not at all acceptable, 100=totally acceptable).[1]

General Acceptance scores significantly improved from Baseline at Weeks 24 and 48 for both treatment groups, after adjusting for baseline score, sex at birth, age, race (white, non-white). No significant differences between the every-8-week and every-4-week CAB + RPV LA groups in adjusted mean change from baseline in treatment acceptance were observed at any timepoint. See Table 6 below.

Table 6. Change from Baseline in General Acceptance Score by Visit (ITT-E Population Without Prior Exposure to CAB + RPV LA) in ATLAS-2M[1]

Visit	Treatment	n	Adjusted Mean (95% CI)*	Adjusted Mean Difference (95% CI)	*P*-value
Week 24	Every 8 weeks	319	5.8 (3.2, 8.5)	1.7 (-2.1, 5.4)	0.379
	Every 4 weeks	323	4.2 (1.5, 6.8)		
Week 48	Every 8 weeks	319	6.8 (4.3, 9.3)	1.1 (-2.4, 4.6)	0.525
	Every 4 weeks	324	5.7 (3.2, 8.1)		

*adjusted for baseline score, sex, age, and race.

ITT-E = intent-to-treat-exposed; CAB + RPV LA = long-acting cabotegravir and rilpivirine; HIVTSQc = HIV Treatment Satisfaction Questionnaire Change Version; CI = confidence interval

Mean (SD) General Acceptance scores for subjects **with prior exposure** to CAB + RPV LA (≥1 weeks) were high at Baseline (89.3 [20.03] points for the every-8-week group and 91.2 [16.74] points for the every-4-week group) and remained stable across Weeks 24 and 48 after adjusting for baseline score, sex at birth (female, male), age (<50, ≥50 years), race (white, non-white), and prior exposure to CAB + RPV LA (1 to 24, >24 weeks), without significant differences between the two treatment groups.[1] See Table 7 below.

Table 7. Change from Baseline in General Acceptance Score by Visit (ITT-E Population With Prior Exposure to CAB + RPV LA) in ATLAS-2M[1]

Visit	Treatment	n	Adjusted Mean (95% CI)*	Adjusted Mean Difference (95% CI)	*P*-value
Week 24	Every 8 weeks	192	-0.4 (-3.0, 2.2)	0.5 (-3.2, 4.2)	0.772
	Every 4 weeks	194	-1.0 (-3.5, 1.6)		
Week 48	Every 8 weeks	192	-1.0 (-3.9, 2.0)	0.9 (-3.2, 5.1)	0.659
	Every 4 weeks	194	-1.9 (-4.8, 1.1)		

*adjusted for baseline score, sex, age, race, and prior exposure to CAB + RPV LA.

ITT-E = intent-to-treat-exposed; CAB + RPV LA = long-acting cabotegravir and rilpivirine; HIVTSQc = HIV Treatment Satisfaction Questionnaire Change Version; CI = confidence interval

PiN

The PiN questionnaire does not produce a total score but consists of 4 dimensions and 5 individually reported items.[1] Pre-specified statistical testing for improvement over time in scores was performed for the dimension of Acceptance of injection site reactions (ISRs) only to avoid multiplicity adjustment. Acceptance of ISRs dimension consists of two items: acceptance of local reactions and acceptance of pain. Responses for each question are rated on a scale of 5 (not at all acceptable) to 1 (totally acceptable), so lower scores indicate greater acceptance.

Both treatment groups reported high initial acceptance of pain and acceptance of local reactions at Week 8 (81% and 68% of subjects rated acceptance of local reactions and pain, respectively, as totally or very acceptable in the every-8-week group at Week 8; 82% and 69% of subjects rated acceptance of local reactions and pain, respectively, as totally or very acceptable in the every-4-week group at Week 8).[1] A statistically significant improvement from Week 8 to Weeks 24 and 48 in the Acceptance of ISRs dimension was observed in the every-4-week and every-8-week groups. See Table 8 below.

No statistical difference in adjusted mean change from Week 8 to Weeks 24 and 48 in Acceptance of ISRs was observed between treatment groups.

Table 8.Summary and Statistical Analysis of Acceptance of ISRs Domain by Visit (ITT-E Population; LOCF) in ATLAS-2M[1]

	Week	n	Median (min, max)	*P* value
Every 8 week group	8	514	2.00 (1.0, 5.0)	N/A
	24	515	1.5 (1.0, 5.0)	0.004
	48	515	1.5(1.0, 5.0)	<0.001
Every 4 week group	8	515	2.0 (1.0, 5.0)	N/A
	24	515	1.5 (1.0, 5.0)	0.002
	48	515	1.5 (1.0, 5.0)	<0.001

ISRs = injection site reactions; ITT-E = intent-to-treat-exposed; LOCF = last observation carried forward

HAT-QoL (short form)

The HAT-QoL instrument originally contained 42 items, grouped into nine dimensions, assessing overall function and well-being.[6] For the purposes of this study, a shorter version adapted from the original was used. This shorter version contains 14 items grouped into the following 3 dimensions: Life Satisfaction, Disclosure Worries, and HIV Medication.

Life Satisfaction

For the Life Satisfaction dimension, scores range from 0 (none of the time) to 100 (all of the time), with higher scores indicating higher satisfaction.

Life Satisfaction scores for subjects in both treatment groups were high at baseline (85.9 points in the every-8-week group and 84.5 points in the every-4-week group for subjects **without prior exposure** to CAB + RPV LA; 85.2 points in the every-8-week group and 89.2 points in the every-4-week group for subjects **with prior exposure**), and remained generally stable across all visits, irrespective of prior CAB + RPV LA exposure, with no significant changes from baseline after adjusting for prespecified covariates at Weeks 24 and 48.[1] When comparing between the two groups for adjusted change from baseline in Life Satisfaction scores, a slight difference in favor of every-4-week dosing compared with every-8-week dosing was observed in the group with prior exposure to CAB + RPV LA, and in favor of the every-8-week group versus the every-4-week group for subjects with prior exposure reaching significance at Week 24 but not at Week 48. These differences were small and may not be clinically meaningful.

Disclosure Worries

For the Disclosure Worries dimension, scores range from 0 (all of the time) to 100 (none of the time), with higher scores indicating fewer disclosure worries.

Disclosure Worries scores for subjects in both treatment groups, irrespective of prior CAB + RPV LA exposure, remained generally stable from baseline (65.3 points in the every-8-week group and 65.7 points in the every-4-week group for subjects **without prior exposure** to CAB + RPV LA; 66.8 points in the every-8-week group and 69.0 points in the every-4-week group for subjects **with prior exposure**) across all visits, with no significant changes after adjusting for prespecified covariates at Weeks 24 and 48.[1] No significant difference was observed between the two groups in adjusted change from baseline in Disclosure Worries scores at any timepoint for subjects with or without prior CAB + RPV LA exposure.

Medication Concerns

For the Medication Concerns dimension, scores range from 0 (all of the time) to 100 (none of the time), with higher scores indicating fewer medication concerns.

Medication Concerns scores for subjects with and without prior exposure to CAB + RPV LA remained relatively stable from baseline (91.6 points in the every-8-week group and 90.2 points in the every-4-week group for subjects **without prior exposure** to CAB + RPV LA exposure; 95.0 points in the every-8-week group and 92.5 points in the every-4-week group for subjects **with prior exposure**) following adjustment for prespecified covariates, with minor numerical improvements at Weeks 24 and 48 for both treatment groups.[1] No statistically significant differences between treatment groups were observed at Weeks 24 and 48 for subjects **with prior exposure** to CAB + RPV LA and Week 24 for subjects **without prior exposure** to CAB + RPV LA. A small significant difference between the every-8-week and every-4-week groups, in favor of the every-8-week group in adjusted change from Baseline in HIV Medication score was observed at Week 48 in subjects without prior exposure.

Preference

Patients in ATLAS-2M were asked the following question:[1]

> "For the past year, you have been receiving long acting injectable medication for the treatment of HIV. Today, we would like you to compare your experience using the long acting injectable medication with your experience taking the oral medication of cabotegravir + rilpivirine you received during the oral lead in phase of the ATLAS (or ATLAS-2M*) study. Based on your experience, which HIV treatment do you prefer?"

*Actual wording included either ATLAS or ATLAS-2M, depending on whether participants transitioned to ATLAS-2M from ATLAS or off-study.

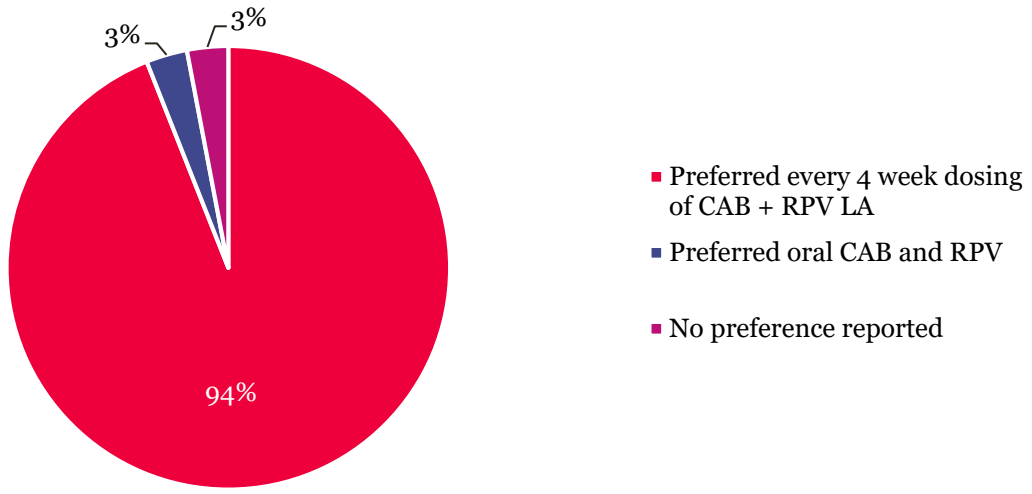
Participants had the option of selecting either "Injectable long-acting HIV treatment every 4 weeks," "Injectable long-acting HIV treatment every 8 weeks," "Oral daily HIV treatment," or "Have no preference."[1]

Every-4-Week Group

Aggregate results were reported for subjects randomized to the every-4-week group, so this group contains subjects who had previously received the every-4-week CAB+RPV LA regimen before rolling into ATLAS 2-M, and subjects who were new to CAB+RPV LA in ATLAS-2M. None of these subjects had experience with every-8-week CAB+RPV LA.

At Week 48, of subjects randomized to the every-4-week treatment group (N=523) with recorded response to the preference question (n=497), 94% (468/497) preferred every-4-week dosing of CAB + RPV LA, regardless of whether or not they had previously received treatment with every-4-week CAB +RPV LA before ATLAS-2M.[1] See Figure 1 below.

Figure 1. Patient Preference (ITT-E Population; with a Recorded Response) in the Every-4-Week Group in ATLAS-2M[1]



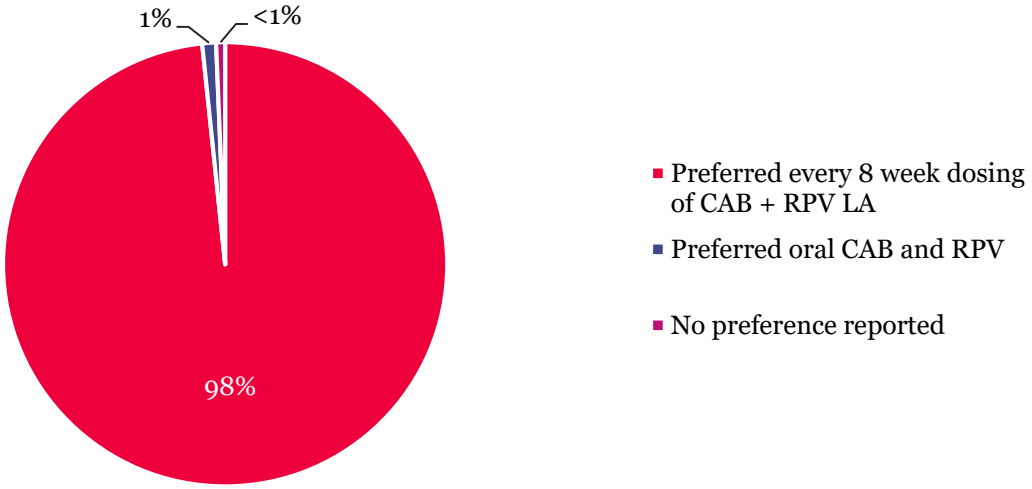
ITT-E = intent-to-treat-exposed; CAB + RPV LA = long-acting cabotegravir and rilpivirine; CAB = cabotegravir; RPV = rilpivirine

Every-8-Week Group

Treatment preference results for the every-8-week group were stratified by prior exposure to CAB + RPV LA.[1]

At Week 48, of subjects randomized to the every-8-week treatment group **without prior exposure** to CAB + RPV LA (N=327) with recorded response to the preference question (n=306), 98% (300/306) preferred every-8-week dosing of CAB + RPV LA.[1] See Figure 2 below.

Figure 2. Patient Preference (ITT-E Population; with a Recorded Response) in the Every-8-Week Group (Without Prior Exposure to CAB + RPV LA) in ATLAS-2M[1]

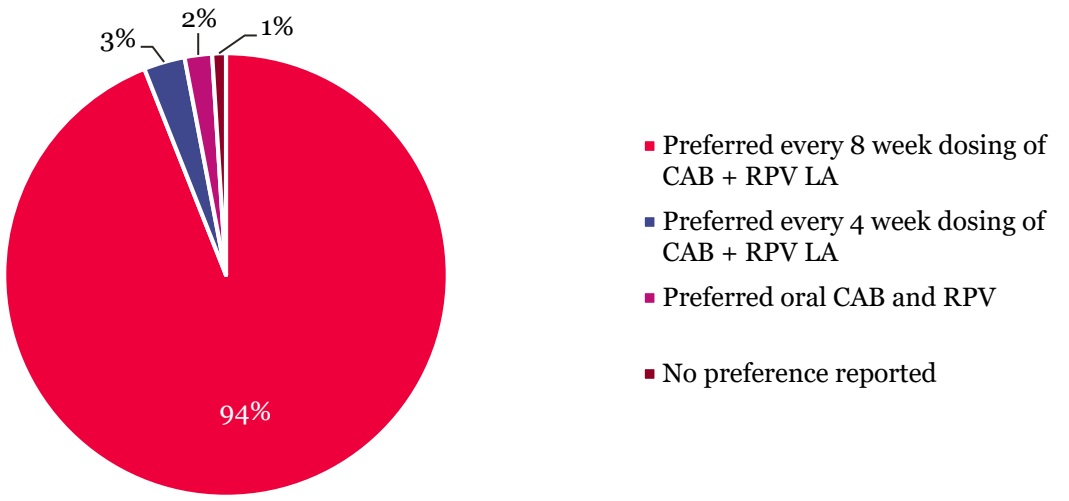


ITT-E = intent-to-treat-exposed; CAB + RPV LA = long-acting cabotegravir and rilpivirine; CAB =cabotegravir; RPV = rilpivirine

At Week 48, of subjects randomized to the every-8-week treatment group **with prior exposure** to the every-4-week CAB + RPV LA regimen (N=195) and with recorded response to the preference question

(n=191), 94% (179/191) preferred every-8-week dosing of CAB + RPV LA compared with 3% (6/191) preferring every-4-week dosing and 2% (4/191) preferring oral CAB + RPV.[1] See Figure 3 below.

Figure 3. Patient Preference (ITT-E Population; with a Recorded Response) in the Every-8-Week Group (With Prior Exposure to CAB + RPV LA) in ATLAS-2M[1]



ITT-E = intent-to-treat-exposed; CAB + RPV LA = long-acting cabotegravir and rilpivirine; CAB = cabotegravir; RPV = rilpivirine

The most common practical attribute of regimen that supported patients' preference in each of the groups highlighted above was the frequency of administration.[1]

The most common main benefit of a regimen that supported patients' preference was that the regimen was more convenient.[1]

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This response was developed according to the principles of evidence-based medicine and, therefore, references may not be all-inclusive.

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