British Columbia Centre *for* Excellence *in* HIV/AIDS

Poster # 84

Tolerability of lopinavir/ritonavir liquid in HIV-positive adults switched from the soft-gel capsule (SGC) formulation

J Toy[1], M Harris[2], J da Silva[1], B Yip[3] and JSG Montaner[3]

[1]Outpatient Pharmacy, St. Paul's Hospital, Vancouver, Canada; [2]AIDS Research Program, St. Paul's Hospital, Vancouver, Canada; [3]BC Centre for Excellence in HIV/AIDS, Vancouver, Canada

Background

Lopinavir/ritonavir (LPV/r) is listed in HIV infection treatment guidelines as a preferred protease inhibitor for antiretroviral-naive patients.[1,2] It is available as a soft gelatin capsule (SGC) containing lopinavir 133.3 mg and ritonavir 33.3 mg, and as an oral solution containing lopinavir 80 mg and ritonavir 20 mg per millilitre. A new tablet formulation obtained US FDA approval in November 2005. The SGC has been associated with gastrointestinal (GI) side effects and increased interest in once-daily regimens has posed an additional tolerability challenge for SGC.[3] Lopinavir/ritonavir liquid has similar pharmacokinetics to SGC under nonfasting moderate fat meal conditions[4] and differences in composition between the two formulations may contribute to a difference in tolerability. There is limited information on the tolerability of the lopinavir/ritonavir oral solution as an alternative to SGC in adults.

Objectives

To assess the tolerability of lopinavir/ritonavir oral solution as part of combination HIV therapy

1. In patients switched from the SGC
2. In patients naïve to lopinavir/ritonavir

Methods

- Observational data were collected at an adult outpatient HIV clinic between October 2005 and July 2006 on
  - Group 1: Patients who had received a lopinavir/ritonavir SGC-containing regimen for at least one month and were offered a switch to liquid formulation
  - Group 2: Patients naïve to lopinavir/ritonavir and were offered liquid formulation as first experience on the medication
- Patients received counseling by clinical pharmacist and were offered a "taste test" of the liquid.
- Minimum follow-up time was 4 weeks (or time of discontinuation).
- Follow-up every 4 weeks included patient self-report of adverse drug reactions and tolerability.

Limitations

- Effect of concomitant medication use not evaluated.
- Pharmacokinetics and efficacy after switch not evaluated.

Results

Group 1: Switch patients

45 were offered the switch to oral solution

- 7 patients (16%) declined citing
  - inconvenience of the liquid formulation 3 (7%)
  - unpleasant taste 4 (9%)

- Baseline GI symptoms reported in 28/38 patients (74%)
- Primary reason given for the switch
  - GI symptoms (i.e. diarrhea, nausea, abdominal distension) 25 (66%)
  - desire for a tolerable once-daily regimen 13 (34%)

Table 1: Group 1 Demographics

Median Age	43 years (31-73)
Sex (% male)	96%
Median CD4+ count	350 cells/μL (40-810)
Median HIV-1 plasma viral load	<50 copies/mL (undetectable - >100,000)

Table 2

Liquid regimen prescribed	Baseline SGC regimen	Reported change in GI symptoms				Discontinuations		
		Improved	Same	Worse	Unavailable	Patients	Median time to stopping (days)	Reason
Once daily (24)	QD = 2 BID=22	5 (21%)	10 (42%)	6 (25%)	3 (12%)	16 (67%)	65 (5-180)	Unpleasant taste (8), inconvenience (1), worsened GI symptoms (4), other (3)
Twice daily (14)	QD = 0 BID=14	5 (36%)	6 (43%)	3 (21%)	0	9 (64%)	33 (6-178)	Unpleasant taste (2), inconvenience (5), worsened GI symptoms (2)
Total (38)	QD = 2 BID= 36	10 (26%)*	16 (42%)	9 (24%)	3 (8%)	25 (66%)	64 (5-180)	

*Improvement in GI symptoms was reported to occur within 2 weeks.

Group 2: LPV/r naive patients

22 patients were offered the oral solution

- 3 patients (14%) declined citing
  - inconvenience of the liquid formulation 1 (5%)
  - unpleasant taste 2 (9%)

- Baseline GI symptoms reported in 9/19 patients (47%)
- Antiretrovirals (ARVs) at baseline
  - ARV naive 4 (21%)
  - Experienced off treatment 8 (42%)
  - Switching regimen 7 (37%)

Table 3: Group 2 Demographics

Median Age	43 years (25-55)
Sex (% male)	95%
Median CD4+ count	200 cells/μL (<10-880)
Median HIV-1 plasma viral load	1830 copies/mL (undetectable - >100,000)

Table 4

Liquid regimen prescribed	ARVs at baseline	Reported change in GI symptoms				Discontinuations		
		Improved	Same	Worse	Unavailable	Patients	Median time to stopping (days)	Reason
Once daily (16)	No=11 Yes=5*	2 (12%)	4 (25%)	7 (44%)	3 (19%)	14 (88%)	24 (4-202)	Unpleasant taste (4), inconvenience (2), worsened GI symptoms (4), other (2), unavailable (2)
Twice daily (3)	No=1 Yes=2**	0	1 (33%)	2 (67%)	0	3 (100%)	36 (26-96)	Inconvenience (1), worsened GI symptoms (1), other (1)
Total (19)	No=12 Yes=7	2 (11%)	5 (26%)	9 (47%)	3 (16%)	17 (89%)	31 (4-202)	

* Nevirapine-based regimen (1), RTV-boosted regimen (4)
** Nelfinavir-based regimen (1), RTV-boosted regimen (1)

Conclusions

Following a switch from lopinavir/ritonavir capsules to liquid, GI side effects improved in 26% and worsened in 24%, and 66% discontinued. Patients naive to lopinavir/ritonavir were less likely to remain on the liquid formulation (89% discontinued). Unpleasant taste, inconvenience and GI symptoms limited the use of this alternative dosage form.

References

1. Hammer SM, Saag MS, Schechter M, Montaner JSG, et al. Treatment for adult HIV infection: 2006 recommendations of the International AIDS Society – USA panel. JAMA. Aug 16, 2006;296(7):827-843.
2. The Panel on Clinical Practices for Treatment of HIV Infection convened by the Department of Health and Human Services (DHHS). Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents. May 4, 2006 http://AIDSinfo.nih.gov (accessed August 15, 2006).
3. Johnson MA, Gathe JC Jr., et al. A once-daily lopinavir/ritonavir-based regimen provides noninferior antiviral activity compared with a twice-daily regimen. J Acquir Immune Defic Syndr. 2006 Aug31; [Epub ahead of print] .
4. Gustavson LE, Lam WV, Bertz RJ, et al. Assessment of the bioequivalence and food effects for liquid and soft elastic capsule co-formulations of ABT-378/ritonavir (ABT-378/r) in health subjects. 40th Interscience Conference on Antimicrobial Agents and Chemotherapy. September 17-20,2000; Toronto.

British Columbia Centre for Excellence in HIV/AIDS

Providence Health Care — How you want to be treated.

Providence Health Care Research Institute