Appendix 4

BHIVA Treatment Guideline update 2013

Search protocol: main databases search: rilpivirine and elvitegravir

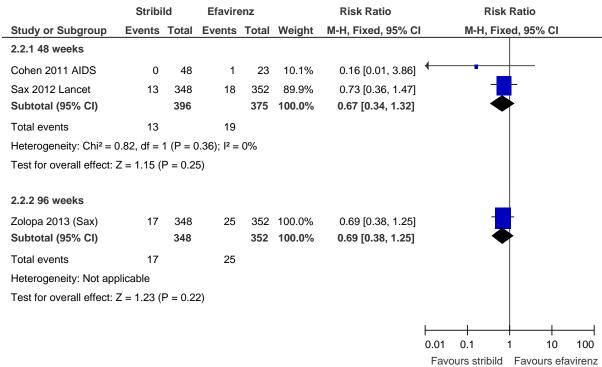
Component	Description						
Review area	New antiretroviral agents – efficacy and safety						
Objectives	Safety and efficacy of rilpivirine and elvitegravir						
Populations	HIV infected, naïve to ART						
	Adults – all questions						
Interventions	Rilpivirine						
	Elvitegravir						
Comparisons/aspects	Both agents with Truvada ,+/- cobicistat (not in search terms) Truvada and efavirenz; ritonavir/atazanavir; any other ART regimens						
covered by search	Truvada and elavirenz, nionavii/alazanavii, any other Arti regimens						
	(terms not in search)						
Outcomes	To be decided by writing groups to include:						
	Virological suppression to <50 copies/mL, virological failure, discontinuation due						
	to AEs, grade 3/4 AEs, HIV drug resistance						
Study designs	All studies						
Exclusions	Animal studies, letters, editorials, comments, non-English studies						
How the information was	Databases: Medline, Embase, Cochrane Library						
searched	Language: restrict to English only						
	Date parameters: 2011 to current						
Search terms and date searched	HIV + (rilpivirine OR elvitegravir)						
	Medline = 121						
	Embase = 130						
Search results	Cochrane = 11						
	Total=262						
	Total deduplicated = 185						

Forest plot of comparison: 2 Stribild versus efavirenz, outcome: 2.1 Confirmed virological response (<50 copies/mL).

	Stribi	Stribild Efa		enz	Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	M-H, Fixed, 95% CI
2.1.1 48 weeks							
Cohen 2011 AIDS	43	48	19	23	8.1%	1.08 [0.88, 1.34]	
Sax 2012 Lancet	299	348	293	352	91.9%	1.03 [0.97, 1.10]	· ·
Subtotal (95% CI)		396		375	100.0%	1.04 [0.98, 1.10]	•
Total events	342		312				
Heterogeneity: Chi ² = 0	0.19, df =	1 (P = 0	0.66); I ² =	0%			
Test for overall effect:	Z = 1.16 (I	P = 0.2	5)				
2.1.2 96 weeks							_
Zolopa 2013 (Sax)	292	348	289	352	100.0%	1.02 [0.96, 1.09]	_
Subtotal (95% CI)		348		352	100.0%	1.02 [0.96, 1.09]	*
Total events	292		289				
Heterogeneity: Not app	olicable						
Test for overall effect:	Z = 0.64 (1	P = 0.5	2)				
2.1.3 144 weeks							_
Study 102	279	348	265	352	100.0%	1.06 [0.98, 1.15]	
Subtotal (95% CI)		348		352	100.0%	1.06 [0.98, 1.15]	•
Total events	279		265				
Heterogeneity: Not app	olicable						
Test for overall effect:	Z = 1.55 (I	P = 0.1	2)				
							0.5 0.7 1 1.5 2
							0.5 0.7 1 1.5 2 Favours efavirenz Favours stribild

Test for subgroup differences: Chi² = 0.61, df = 2 (P = 0.74), $I^2 = 0\%$

Forest plot of comparison: 2 Stribild versus efavirenz, outcome: 2.2 Discontinued due to adverse event.



Test for subgroup differences: $Chi^2 = 0.00$, df = 1 (P = 0.96), $I^2 = 0\%$

Forest plot of comparison: 2 Stribild versus efavirenz, outcome: 2.3 Virological failure.

	Stribi	ld	Efavire	enz		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	M-H, Fixed, 95% CI
2.3.1 48 weeks							
Cohen 2011 AIDS	0	48	1	23	14.1%	0.16 [0.01, 3.86]	
Sax 2012 Lancet	16	312	12	300	85.9%	1.28 [0.62, 2.66]	-
Subtotal (95% CI)		360		323	100.0%	1.12 [0.56, 2.25]	•
Total events	16		13				
Heterogeneity: Chi ² = 1	.55, df =	1 (P = 0).21); I² =	36%			
Test for overall effect: Z	z = 0.33 (P = 0.7	4)				
2.3.2 96 weeks							
Study 102	22	348	27	352	100.0%	0.82 [0.48, 1.42]	*
Subtotal (95% CI)		348		352	100.0%	0.82 [0.48, 1.42]	•
Total events	22		27				
Heterogeneity: Not appl	licable						
Test for overall effect: Z	z = 0.70 (P = 0.4	9)				
2.3.3 144 weeks							_
Study 102	26	348	34	352	100.0%	0.77 [0.47, 1.26]	
Subtotal (95% CI)		348		352	100.0%	0.77 [0.47, 1.26]	•
Total events	26		34				
Heterogeneity: Not appl	licable						
Test for overall effect: Z	z = 1.03 (P = 0.3	0)				
							0.01 0.1 1 10 100
							Favours stribild Favours efavirenz

Test for subgroup differences: $Chi^2 = 0.78$, df = 2 (P = 0.68), $I^2 = 0\%$

Forest plot of comparison: 3 Stribild versus atazanavir, outcome: 3.1 Confirmed virological response (<50 copies/mL).

	Stribi	ld	Atazan	avir	Risk Ratio			Risk	Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	i .	M-H, Fix	ed, 95% CI	
3.1.1 48 weeks									L	
DeJesus 2012 Lancet	304	353	301	355	100.0%	1.02 [0.96, 1.08]				
Subtotal (95% CI)		353		355	100.0%	1.02 [0.96, 1.08]		•	•	
Total events	304		301							
Heterogeneity: Not applicable	€									
Test for overall effect: $Z = 0.5$	50 (P = 0.6	62)								
3.1.2 96 weeks								_		
Rockstroh 2013 (DeJesus)	293	353	291	355	100.0%	1.01 [0.95, 1.08]				
Subtotal (95% CI)		353		355	100.0%	1.01 [0.95, 1.08]		•		
Total events	293		291							
Heterogeneity: Not applicable	Э									
Test for overall effect: $Z = 0.3$	36 (P = 0.7	72)								
3.1.3 144 weeks										
Study 103	274	353	265	355	100.0%	1.04 [0.96, 1.13]		-	-	
Subtotal (95% CI)		353		355	100.0%	1.04 [0.96, 1.13]		•		
Total events	274		265							
Heterogeneity: Not applicable	Э									
Test for overall effect: $Z = 0.9$	93 (P = 0.3	35)								
							<u> </u>	+	,	
							0.5	0.7	1 1.5	
							Favour	rs atanazavir	Favours stri	bild

Test for subgroup differences: Chi² = 0.27, df = 2 (P = 0.87), I^2 = 0%

Forest plot of comparison: 3 Stribild versus atazanavir, outcome: 3.2 Discontinued due to adverse event.

	Stribi	ld	Atazan	avir		Risk Ratio		Risk	Ratio	
Study or Subgroup					Weight	M-H, Fixed, 95% C	I		ed, 95% CI	
3.2.1 48 weeks										
DeJesus 2012 Lancet	13	353	18	355	100.0%	0.73 [0.36, 1.46]		-	-	
Subtotal (95% CI)		353		355	100.0%	0.73 [0.36, 1.46]		•		
Total events	13		18							
Heterogeneity: Not applicable)									
Test for overall effect: $Z = 0.9$	00 (P = 0.3	37)								
3.2.2 96 weeks										
Rockstroh 2013 (DeJesus)	14	353	21	355	100.0%	0.67 [0.35, 1.30]		-	-	
Subtotal (95% CI)		353		355	100.0%	0.67 [0.35, 1.30]		•		
Total events	14		21							
Heterogeneity: Not applicable)									
Test for overall effect: Z = 1.1	9 (P = 0.2	24)								
								 	 	
							0.01	0.1	1 10	10
							Fa	vours stribild	Favours ata	zana

Test for subgroup differences: $Chi^2 = 0.03$, df = 1 (P = 0.87), $I^2 = 0\%$

Forest plot of comparison: 3 Stribild versus atazanavir, outcome: 3.3 Virological failure.

	Stribi	ld	Atazan	avir	Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	M-H, Fixed, 95% CI
3.3.1 48 weeks							<u>_</u>
DeJesus 2012 Lancet	8	318	7	310	100.0%	1.11 [0.41, 3.04]	-
Subtotal (95% CI)		318		310	100.0%	1.11 [0.41, 3.04]	•
Total events	8		7				
Heterogeneity: Not appli	cable						
Test for overall effect: Z	= 0.21 (P	= 0.83))				
3.3.2 96 weeks							
Study 103	24	353	26		100.0%	0.93 [0.54, 1.58]	T
Subtotal (95% CI)		353		355	100.0%	0.93 [0.54, 1.58]	•
Total events	24		26				
Heterogeneity: Not appli	cable						
Test for overall effect: Z	= 0.27 (P	= 0.79))				
3.3.3 144 weeks							_
Study 103	28	353	26	355	100.0%	1.08 [0.65, 1.81]	
Subtotal (95% CI)		353		355	100.0%	1.08 [0.65, 1.81]	T
Total events	28		26				
Heterogeneity: Not appli	cable						
Test for overall effect: Z	= 0.30 (P	= 0.76))				
							0.01 0.1 1 10 100
							Favours stribild Favours atazanavir

Test for subgroup differences: Chi² = 0.20, df = 2 (P = 0.90), I^2 = 0%