

## Industry Request – Integrase Inhibitors

The objective of this request is to describe and understand the temporal changes in the prescribing practices of Integrase Inhibitors (II) in AHOD cohort between 1/1/2009 and 31/12/2010. The information found in this document will be used to assist planning of educational initiatives and communication of the use of II's.

NOTE: the following points are applicable throughout the document unless clearly stated otherwise.

1. A patient's regimen is classified\* by selecting the combination antiretroviral therapy regimen with the longest duration in each calendar year. Patients lost to follow-up before 1/1/2009 or off-treatment are not included in results presented in this document.

\*the classification of a regimen is based on the individual agents of the regimen. The following classifications are used in AHOD.

### Antiretroviral agent class definition:

II – Integrase Inhibitor

NRTI – Nucleoside/Nucleotide reverse transcriptase inhibitor

NNRTI – Non-nucleoside reverse transcriptase inhibitor

PI – Protease inhibitor

MONO – mono therapy

DUO – dual therapy

<b>Regimen Label</b>	<b>Regimen Description</b>
II	3+ agents, II, ( $\pm$ NRTI $\pm$ NNRTI $\pm$ PI)
NNRTI+PI	3+ agents, NNRTI+PI, ( $\pm$ NRTI, no II)
NRTI	3+ agents, NRTI (no NNRTI, no PI, no II)
NRTI+NNRTI	3+ agents, NRTI+NNRTI (no PI, no II)
NRTI+PI	3+ agents, NRTI+PI (no NNRTI, no II)
MONO/DUO	1 or 2 agents used individually or together

2. Combination antiretroviral therapy (cART) regimens are defined as 3 or more antiretroviral agents initiated after 1/1/1997 and have a duration of usage more than 14 days.
3. Regimen lines (1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>rd</sup>, 4<sup>th</sup>+) are defined by any change to the original cART regimen including substitution of an antiretroviral agent within a class (defined point 1 above) or the addition/initiation of a new class of drug.

Example: Hypothetical treatment pathway as defined by the definition of regimen line used in this document (changes in regimen are **bold**).

<b>Regimen Line</b>	<b>cART Regimen</b>			
1	NRTI_A	NRTI_B	PI_A	
2	NRTI_A	<b>NRTI_C</b>	PI_A	
3	NRTI_A	NRTI_C	PI_A	<b>PI_B</b>
4	<b>NRTI_D</b>	<b>II_A</b>		

**Table 1: What percentage of all II usage falls in the 1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>rd</sup> or 4<sup>th</sup>+ combination therapy regimens.**

Regimen	2009		2010	
	N	(%)	N	(%)
1	29	(13)	40	(12)
2	12	(5)	28	(9)
3	11	(5)	17	(5)
4+	178	(77)	243	(74)
Total	230		328	

**Table 2: What percentage of all treatment at each line of therapy (1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>rd</sup>, 4<sup>th</sup>+) does II account for?**

(a) Patient numbers and percentages.

Regimen	2009				2010			
	Non-II		II		Non-II		II	
	N	(%)	N	(%)	N	(%)	N	(%)
1	348	(92)	29	(8)	343	(90)	40	(10)
2	254	(95)	12	(5)	249	(90)	28	(10)
3	197	(95)	11	(5)	200	(92)	17	(8)
4+	875	(83)	178	(17)	779	(76)	243	(24)

(b) Percentage comparison between 2009 and 2010.

Regimen	Non-II		II	
	2009	2010	2009	2010
	(%)	(%)	(%)	(%)
1	92	90	8	10
2	95	90	5	10
3	95	92	5	8
4+	83	76	17	24

**Table 3: What are the percentages of other anchor agents (i.e. NNRTI+PI, NRTI+PI, etc) in each of the different lines of therapy?**

(a) 2009: number of patients and percentages.

Regimen	II		NNRTI+PI		NRTI		NRTI+NNRTI		NRTI+PI		MONO/DUO		Total N
	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	
1	29	(8)	5	(1)	7	(2)	248	(66)	88	(23)	0	(0)	377
2	12	(5)	11	(4)	7	(3)	169	(64)	62	(23)	5	(2)	266
3	11	(5)	14	(7)	9	(4)	113	(54)	52	(25)	9	(4)	208
4+	178	(17)	90	(9)	9	(1)	305	(29)	407	(39)	64	(6)	1053

(b) 2010: number of patients and percentages.

Regimen	II		NNRTI+PI		NRTI		NRTI+NNRTI		NRTI+PI		MONO/DUO		Total N
	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	
1	40	(10)	4	(1)	6	(2)	234	(61)	99	(26)	0	(0)	383
2	28	(10)	9	(3)	5	(2)	166	(60)	63	(23)	6	(2)	277
3	17	(8)	13	(6)	6	(3)	122	(56)	52	(24)	7	(3)	217
4+	243	(24)	78	(8)	9	(1)	289	(28)	352	(34)	51	(5)	1022

(c) Comparison between 2009 and 2010.

Regimen	II		NNRTI+PI		NRTI		NRTI+NNRTI		NRTI+PI		MONO/DUO	
	2009 (%)	2010 (%)	2009 (%)	2010 (%)	2009 (%)	2010 (%)	2009 (%)	2010 (%)	2009 (%)	2010 (%)	2009 (%)	2010 (%)
1	8	10	1	1	2	2	66	61	23	26	0	0
2	5	10	4	3	3	2	64	60	23	23	2	2
3	5	8	7	6	4	3	54	56	25	24	4	3
4+	17	24	9	8	1	1	29	28	39	34	6	5

**Table 4: What treatment grouping is switched away from when an II is introduced in the 2<sup>nd</sup>, 3<sup>rd</sup> or 4<sup>th</sup>+ combination regimens.**

**NOTE: To reduce the total number of possible cART combinations and to avoid direct head-to-head comparison of individual agents, the following groupings are used.**

Group Label	Antiretroviral Therapy Agents
NRTI	abacavir, combivir, didanosine, lamivudine, stavudine, trizivir, zalcitabine, zidovudine, hydroxyurea, emtricitabine, truvada, kivexa, apricitabine, adefovir, tenofovir, enfuvirtide, IL-2
NNRTI_1 NNRTI_2	efavirenz, etravirine nevirapine, delavirdine
PI_1 PI_2 PI_3	atazanavir, darunavir kaletra, saquinavir amprenavir, indinavir, nelfinavir, ritonavir, tipranavir, fosamprenavir, lopinavir
OTHER	maraviroc, trial drug

(a) 2009, regimen switched away from to an II based combination. Regimens where only 1 person switched are not shown.

Regimen Number^	II regimen switched to from a non-II regimen*	Number of Patients
2	NNRTI_1/NRTI	2
	NNRTI_2/NRTI	2
	NNRTI_2/NRTI/NRTI	2
	NNRTI_2/NRTI/PI_2	2
	Not Shown	4
3	NNRTI_1/NRTI	4
	NRTI/NRTI/PI_1/PI_3	3
	NNRTI_1/NRTI/NRTI/PI_3/PI_3	2
	Not Shown	8

4+	NRTI/NRTI/PI_1/PI_3	21
	NRTI/NRTI/PI_2	15
	NRTI/PI_1/PI_3	14
	NRTI/PI_2	13
	NNRTI_2/NRTI	9
	NRTI/NRTI/NRTI/PI_1/PI_3	8
	NRTI/PI_1	8
	NNRTI_2/NRTI/NRTI	7
	NRTI/NRTI	7
	NRTI/PI_3/PI_3	7
	NNRTI_1/NRTI/NRTI	6
	NRTI/NRTI/NRTI	5
	NRTI/NRTI/PI_3/PI_3	5
	NRTI/NRTI/PI_1	4
	NRTI/NRTI/PI_3	4
	NRTI/PI_3	4
	NNRTI_1/NRTI	3
	NNRTI_1/NRTI/NRTI/NRTI	3
	NNRTI_2/NRTI/PI_1/PI_3	3
	NRTI	3
	NRTI/PI_2/PI_3	3
	NNRTI_1/NRTI/NRTI/PI_1/PI_3	2
	NNRTI_1/NRTI/PI_1/PI_3	2
	NRTI/NRTI/NRTI/OTHER/PI_1/PI_3	2
	NRTI/NRTI/NRTI/PI_2	2
	NRTI/NRTI/OTHER/PI_2	2
	NRTI/NRTI/PI_1/PI_2	2
	NRTI/OTHER/PI_1/PI_3	2
	NRTI/PI_1/PI_2	2
	NRTI/PI_2/PI_2	2
	PI_1/PI_2	2
	PI_1/PI_2/PI_3	2
	Not Shown	31

^as defined when initiating II regimen.

\*regimen components have been reclassified as per the definitions outlined in Table 4 description.

(b) 2010, regimen switched away from to an II based combination. Regimens where only 1 person switched are not shown.

Regimen Number^	Non-II regimen switched away from to a II regimen*	Number of Patients
2	NRTI/PI_1/PI_3	6
	NRTI/PI_2	4
	NNRTI_2/NRTI	2
	Not Shown	10
3	NNRTI_2/NRTI	3
	NRTI/NRTI/PI_1/PI_3	2
	NRTI/PI_1/PI_3	2
	Not Shown	5
4+	NRTI/NRTI/PI_1/PI_3	7
	NRTI/PI_1/PI_3	7
	NRTI/NRTI/PI_2	6
	NRTI/PI_2	5
	NNRTI_2/NRTI	4
	NNRTI_1/NRTI	3
	NNRTI_1/NRTI/PI_2	3
	NNRTI_1/NRTI/NRTI	2
	NNRTI_2/NRTI/NRTI	2
	NNRTI_2/NRTI/PI_2	2
	NRTI/NRTI	2
	NRTI/NRTI/PI_1	2
	NRTI/NRTI/PI_3/PI_3	2
	Not Shown	15

^as defined when initiating II regimen.

\*Regimen components have been reclassified as per the definitions outlined in Table 4 description.

**Table 5: What are the top 5 combination regimens utilizing II?**

(a) 2009 top 5 II regimens

<b>Integrase Inhibitor Regimen</b>	<b>Number of Patients</b>
Truvada/Raltegravir	26
Atazanavir/Raltegravir	10
Truvada/Ritonavir/Darunavir/Raltegravir	9
Emtricitabine/Tenofovir/Raltegravir	7
Etravirine/Ritonavir/Darunavir/Raltegravir	7

(b) 2010 top 5 II regimens

<b>Integrase Inhibitor Regimen</b>	<b>Number of Patients</b>
Truvada/Raltegravir	37
Atazanavir/Raltegravir	15
Etravirine/Ritonavir/Darunavir/Raltegravir	13
Kaletra/Raltegravir	10
Emtricitabine/Tenofovir/Raltegravir	9
Truvada/Ritonavir/Darunavir/Raltegravir	9
Ritonavir/Darunavir/Raltegravir	9

**Table 6: What treatment grouping is switched to, if II are discontinued?**

(a) 2009, switches from an II based regimen. Regimens where only 1 person switched are not shown.

<b>Regimen Number</b>	<b>Regimen switched to from an II regimen*</b>	<b>Number of Patients</b>
1		0
2		0
3		0
4+	NRTI/NRTI/PI_1/PI_3	2
	Not Shown	4

(b) 2010, switches from an II based regimen. Regimens where only 1 person switched are not shown.

<b>Regimen Number</b>	<b>Regimen switched to from an II regimen*</b>	<b>Number of Patients</b>
1	Not shown	1
2	Not shown	1
3	NNRTI_1/NRTI	2
4+	NNRTI_1/NRTI	2
	NRTI/NRTI/PI_2	2
	Not shown	6

\*Regimen components have been reclassified as per the definitions outlined in Table 4 description.