The impact of product ‘switch’ on risk of inhibitor development in Australian HMA patients

Simon McRae, Ann Wilson, Huyen Tran.

17th ANZ Conference on Haemophilia & related Bleeding Disorders, Gold Coast 2015

Introduction:

- Management of patients with inhibitors is complex

- Major issues include:
  - Frequent bleeding episodes
  - Disabling arthropathy
  - Shorter life expectancy
  - Substantially reduced quality of life

- Risk factors include:
  - Genotype
  - Family history
  - Treatment-related (intensity & frequency)

Although there is a lack of compelling evidence, there is some ongoing concern that switching of treatment product can result in inhibitor development.

(Iorio et al, 2012, Blood 120(4): 720-727)

Previous inhibitor studies show

Study	Country	Switch to product	Population evaluated	Patients enrolled	Patients evaluated	Severe HMA n (%)	Positive for inhibitors at baseline (preswitch) n (%)	Inhibitor detection (post-switch) n (%)
Bacon et al, 2011	Ireland	ADVATE®	Switch	113	113	101 (89)	2 (1.7)	1 (0.9)
Rubinger et al, 2008	Canada	Kogenate®	Switch	460	274	220 (89)	4 (1.5)	4 (1.5)
Hay et al, 2012	UK	ReFacto AF®	Switch/non-switch	1217	535/682	1217 (100)	0	4(0.75)/ 1 (0.1)

(Taken from Santagastino et al, 2014 European J Haematology 94: 284-289)

Aim:

To evaluate the impact of product ‘switch’ on inhibitor development among Australian patients with Haemophilia A, who were recently involved in treatment product switching due to the National Tender Process.

Method:

Group 1: ADVATE® - Kogenate®

(n = 533)

Switch product

(n = 237)

Inhibitor test 1

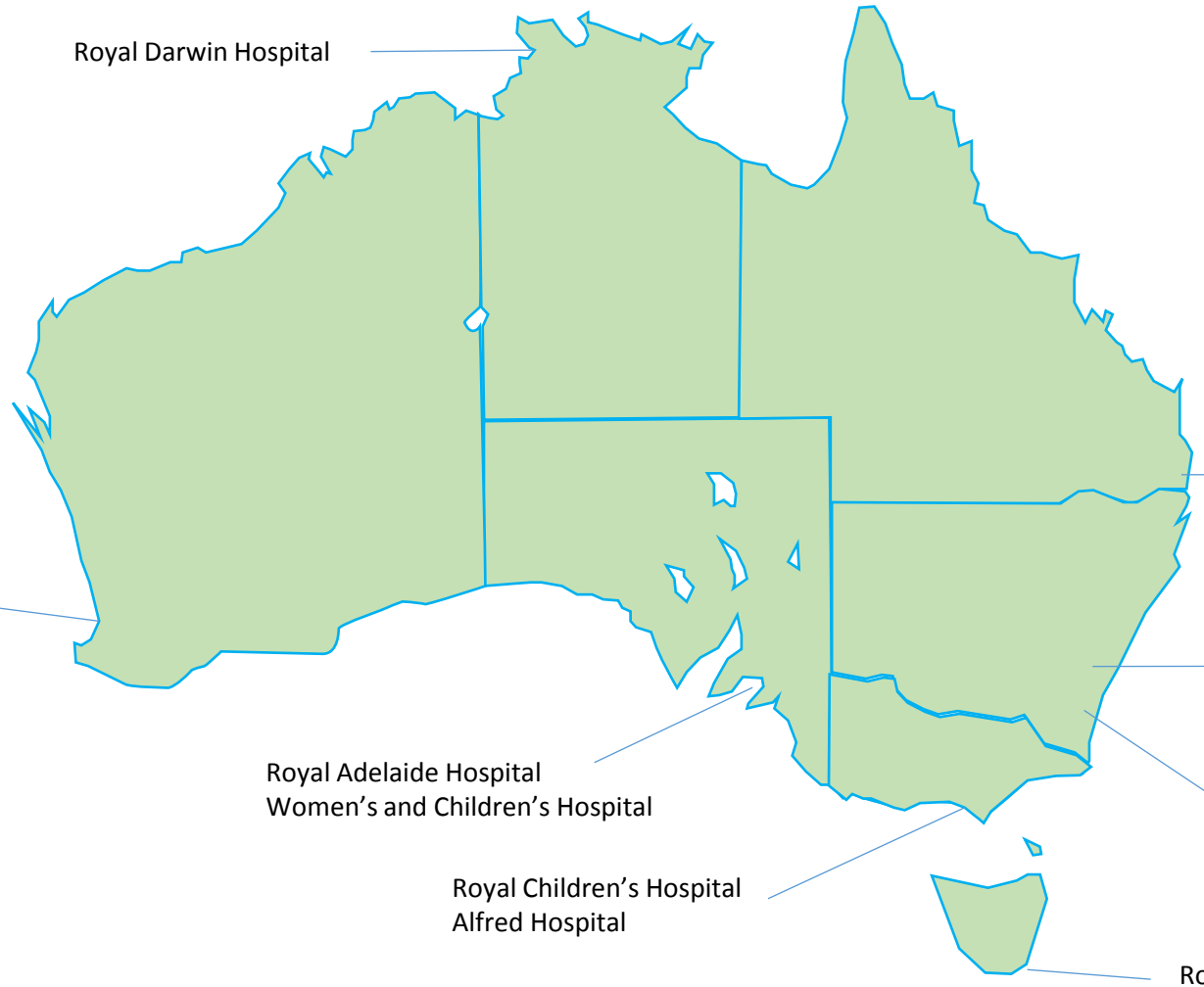
Inhibitor test 2

Group 2: Control

(n = 114)

No switch

(n = 100)


Royal Darwin Hospital
Lady Cilento Children's Hospital
Royal Brisbane and Women's Hospital
Fiona Stanley Hospital
Princess Margaret Hospital
Sydney Children's Hospital
Westmead Hospital
Children's Hospital at Westmead
Royal Prince Alfred Hospital
Prince of Wales Hospital
Calvary Mater Newcastle
Royal Adelaide Hospital
Women's and Children's Hospital
Canberra Hospital
Royal Children's Hospital
Alfred Hospital
Royal Hobart Hospital

AHCDO

Results 1:

Baseline Patient Characteristics		
Characteristics	Switched	Control
Total subjects	237	100
Gender Male Female	 234 3	 100 0
Median age at switch (range)	29 (3 – 93)	38 (6 – 81)
Severity of disease {n (%)} Mild Moderate Severe	 38 (16%) 27 (11%) 172 (73%)	 28 (28%) 14 (14%) 58 (58%)
Exposure days 1-50 >50	 26 211	

Results 2:

Positive for Inhibitor Patient Characteristics		
Characteristics	Switched	Control
Total positive for inhibitor	3 (1%)	4 (4%)
Gender Male Female	 3 0	 4 0
Median age at switch (range)	23 (5 – 55)	33 (18 – 62)
Severity of disease Mild Moderate Severe	 1 (33%) 0 2 (66%)	 2 (50%) 2 (50%) 0
Median inhibitor titre (range)	1.7 (0.7 – 3.5)	3.6 (1.1 – 8.4)
Exposure days 1-50 >50	 0 3	

Results 3:

	Age	Severity	PTP	Product	Inhibitor result (BU)
Control	18	Mild	On demand	Xyntha®	1.1
	19	Moderate	On demand	Xyntha®	
	32	Moderate	Prophylaxis	Xyntha®	1.3
	62	Mild	On demand	Xyntha®	8.4

	Age	Severity	PTP	Product	Switched product	Time to test (weeks)	Post-switch Inhibitor result (BU)
Switched	5	Severe	>50 EDs	ADVATE®	Kogenate®	48	0.9
	9	Severe	>50 EDs	ADVATE®	Kogenate®	4	0.7
	55	Mild	>50 EDs	ADVATE®	Xyntha®	98	3.5 (3.8)

Limitations:

- Heterogeneous patient population
- Matching controls
- Missing/incomplete data for some switched patients
- Not all positive inhibitors were confirmed with a second test

Conclusion:

Switching of treatment product is **not** associated with **an increased rate of inhibitor development** in the Australian Haemophilia A patient population.

Further Research:

- Matching controls
- Determine any genetic predispositions
- Confirm all inhibitor results with a second test

Acknowledgements:

Acknowledge the collaboration and assistance of:

1. Directors of Haemophilia Treatment Centres nation-wide
2. Individual data managers from each HTC
3. The patient participants