1157

Psoriasis Treatment Progression and Biologic Utilization: A Canadian Retrospective Study

Neil H. Shear, MD, FRCPC[1]; Wendy N. Dobson-Belaire, PhD[2]; Ginger Tey, MASc[2]; Kristen Reidel, MSc[3]; Fei Fei Liu, BSc(Pharm), MBA[4]; Zeba M. Khan, RPh, PhD[5]

[1]Department of Medicine (Dermatology, Clinical Pharmacology), University of Toronto, Toronto, Ontario, Canada and Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada; [2]IMS Brogan, a unit of IMS Health, Mississauga, Ontario, Canada; [3]IMS Brogan, a unit of IMS Health, Kirkland, Québec, Canada; [4]Celgene Inc., Mississauga, Ontario, Canada; [5]Celgene Corporation, Summit, NJ, USA

Presented at: the 73rd Annual Meeting of the American Academy of Dermatology; March 20-24, 2015; San Francisco, CA.

This study was sponsored by Celgene Corporation.

Disclosures

- Dr. NH Shear has received honoraria as a consultant and/or advisory board member of AbbVie, Amgen, Celgene, Janssen, LEO Pharma, Merck, and Novartis.
- Dr. WN Dobson-Belaire, K Reidel, and G Tey are employees of IMS Health, who were paid consultants to Celgene in association with the development of this poster.
- Dr. ZM Khan and FF Liu are employees of Celgene Corporation.

Abstract

Background: Moderate to severe psoriasis accounts for ~21-33% of psoriasis cases and places significant burden on patients and healthcare systems (Lebwohl, 2014; Koo, 1996). A scarcity of comprehensive evidence on treatment progression, persistence, and adherence to medications for moderate to severe psoriasis limits the current understanding of the real-world experience of Canadian psoriasis patients.

Objective: Describe the treatment progression for Canadian psoriasis patients from their first non-biologic systemic (NBS) therapy through biologic (BLx) therapy, generally the last available treatment option.

Methods: This is a retrospective analysis of psoriasis patients within Canadian private and public medication claims databases from October 2007 to September 2013. The role of NBS and BLx medications in treatment progression was described over a 3-year period. Additionally, a study of BLx drug utilization was conducted to evaluate the 3-year persistence and adherence to a patient's first BLx, where adherence is defined as medication possession ratio ≥80%. Cox proportional hazard and logistic regression models were used to assess the impact to persistence and adherence in terms of BLx molecule, age, gender, co-pay, and preexisting medical condition.

Results: A cohort of 5,440 psoriasis patients was identified in this study, where 85% commenced systemic treatment on an NBS therapy and 15% initiated on a BLx agent. Of the first-line NBS patients, 50% discontinued all systemic psoriasis treatment within the study period, while 15% progressed to BLx therapy. Among patients with ≥1 BLx claim (N=1,539), the average 3-year persistence to the first BLx drug was 31%. For patients eligible for the adherence analysis (N=1,485), 45% were adherent to their BLx over 3 years. Multivariate regression analyses suggested preexisting GI disease was associated with better persistence and adherence, whereas females and preexisting respiratory disease were associated with poorer persistence and adherence. Ustekinumab was associated with better adherence but not persistence.

Conclusion: High discontinuation of therapy among psoriasis patients treated with current NBS products suggests potential patient dissatisfaction with pre-BLx treatment options. BLx treatment, often the last available option, shows a similar trend, with 69% of patients discontinuing their first BLx within 3 years of initiation. Thus, a need exists for novel psoriasis treatment strategies.

Introduction and Objective

- Psoriasis is a chronic inflammatory disease that affects 1% to 3% of Canadians.[1]
- Moderate to severe psoriasis accounts for ~30% of psoriasis cases and places significant burden on patients and healthcare systems.[2,3]
- Appropriate drug utilization is essential to obtaining favorable clinical outcomes. This involves both *persistence* (a patient remaining on therapy) and *adherence* (a patient using medication appropriately while on therapy).
- A scarcity of comprehensive evidence on treatment progression, persistence, and adherence to medications for moderate to severe psoriasis limits current understanding of the real-world experience of Canadian psoriasis patients.
- The objectives of this presentation are to:
  - Describe the treatment progression for Canadian psoriasis patients from their first non-biologic systemic (NBS) therapy through biologic (BLx) therapy, generally the last available treatment option.
  - Evaluate and quantify the impact of patient characteristics and medication choice on psoriasis patient persistence and adherence to NBS and BLx therapy in Canada.

1. Papp K, et al. *J Cutan Med Surg*. 2010; 14(4):167-174; 2. Lebwohl MG, et al. *J Am Acad Dermatol.* 2014; 70(5):871-881; 3. Koo J. *Dermatol Clin.* 1996; 14(3):485-496.

Study Design

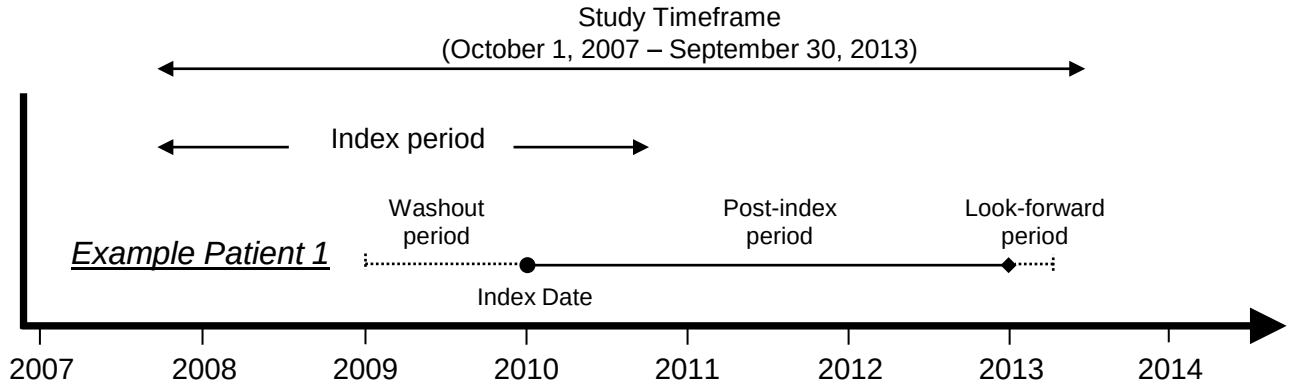
12 months (1 year)	36 months (3 years)	36 months (3 years)	3 months
Washout period	**Index period (October 1, 2007 – September 30, 2010)**	**Post-index period**	**Look-forward period**

Each patient is observed before the index date to assess naïve status to medication classes of interest and describe preexisting comorbid conditions

The date of the first claim for a medication of interest during this period is the patient's index date

Patients are studied for 36 months following their index date to evaluate treatment progression,* persistence,§ and adherence‡

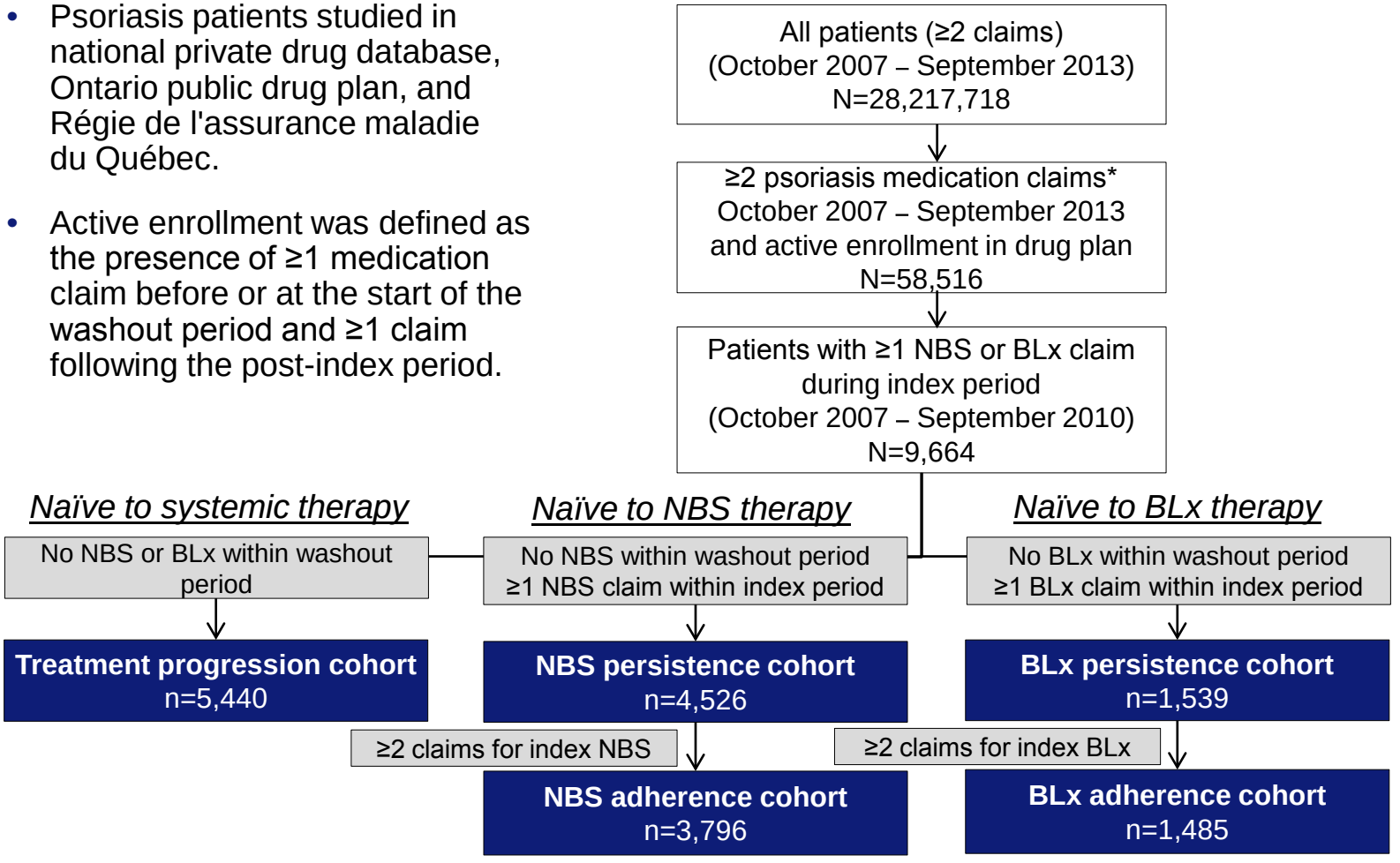
An additional 3-month period is used to classify the patient's last claim (i.e., switch vs. discontinue)



*A new line of treatment was defined as an addition, reduction, or switch of a systemic therapy.
§Discontinuation was defined by the absence of a subsequent claim for the index medication within 60 days following the previous claim.
‡Adherence was defined as a medication possession ratio (MPR) ≥80%.
MPR=(total days supplied during the post-index period)/(number of days in the post-index period).

Patient Selection

- Psoriasis patients studied in national private drug database, Ontario public drug plan, and Régie de l'assurance maladie du Québec.
- Active enrollment was defined as the presence of ≥1 medication claim before or at the start of the washout period and ≥1 claim following the post-index period.



*See Appendix for list of medications to infer psoriasis.

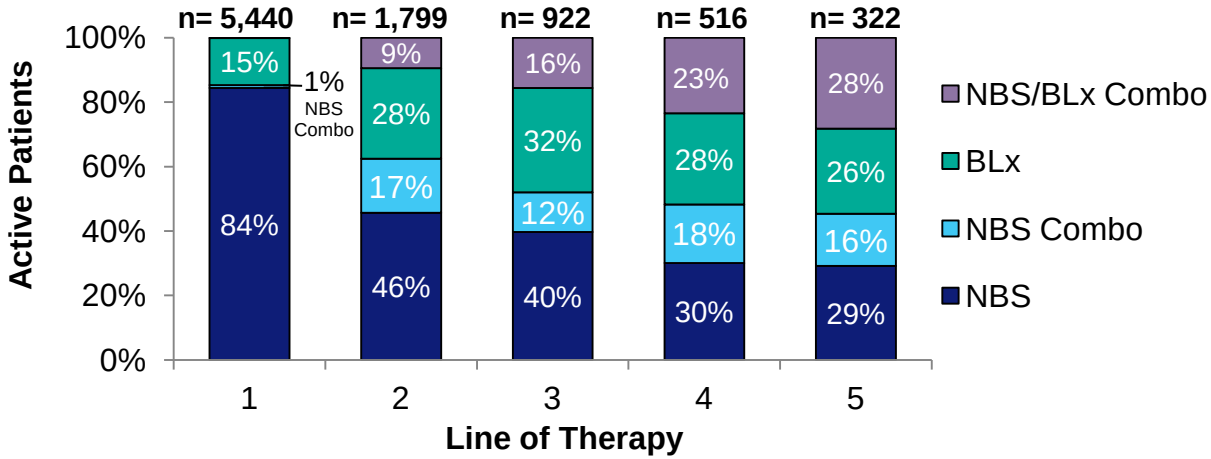
Baseline Patient Demographics and Comorbidity Characteristics

	Treatment Progression	Persistence		Adherence	
		NBS	BLx	NBS	BLx
Patients, n (%)	n=5,440	n=4,526	n=1,539	n=3,796	n=1,485
Age, years*					
<40	918 (17)	689 (15)	366 (24)	585 (16)	358 (24)
40-64	3,270 (60)	2,694 (60)	985 (64)	2,254 (59)	945 (64)
≥65	1,252 (23)	1,143 (25)	188 (12)	957 (25)	182 (12)
Gender					
Male	2,741 (50)	2,229 (49)	848 (55)	1,867 (49)	827 (56)
Female	2,685 (49)	2,297 (51)	691 (45)	1,929 (51)	658 (44)
Unknown	14 (0.3)	0 (0)	0 (0)	0 (0)	0 (0)
Insurance type					
Private	3,581 (66)	2,867 (63)	1,151 (75)	2,390 (63)	1,108 (75)
Public	1,859 (34)	1,659 (37)	388 (25)	1,406 (37)	377 (25)
Preexisting comorbid condition§					
Cardiovascular	2,435 (45)	2,088 (46)	623 (40)	1,758 (46)	597 (40)
Infection	1,430 (26)	1,212 (27)	446 (29)	1,018 (27)	432 (29)
Depression or mood	1,022 (19)	848 (19)	307 (20)	728 (19)	297 (20)
Respiratory	628 (12)	532 (12)	150 (10)	446 (12)	143 (10)
Diabetes	633 (12)	522 (12)	183 (12)	442 (12)	180 (12)
Gastrointestinal	219 (4)	178 (4)	109 (7)	150 (4)	106 (7)

***Mean age cannot be reported due to lack of availability in the Régie de l'assurance maladie du Québec database.
§Comorbidity presence was measured based on indication-specific medication use within the washout period.

Treatment Progression Results

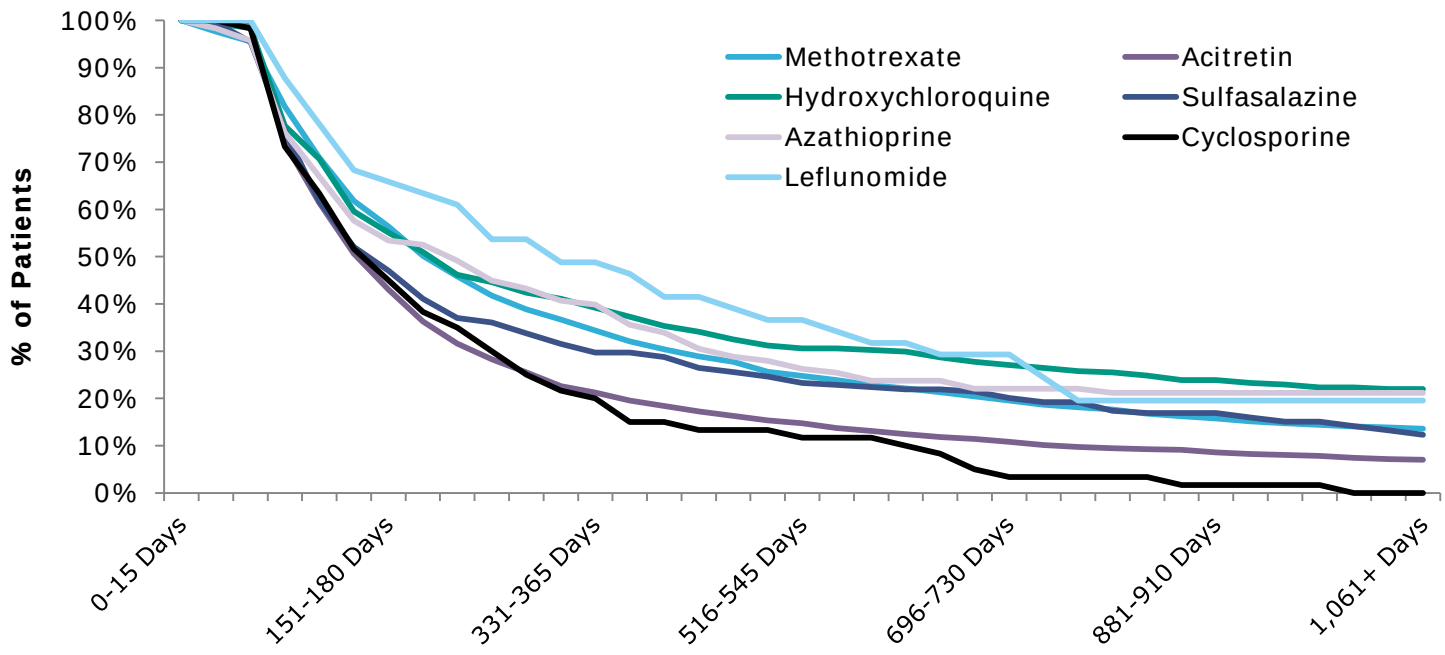
- Within the index period (October 1, 2007 to September 30, 2010), 85% of patients began systemic treatment on an NBS therapy and 15% initiated on a BLx agent.
- Of the patients whose first systemic treatment was an NBS agent, 50% discontinued* all systemic psoriasis treatment within the study period, 35% continued on NBS therapy until the end of the study period, and 15% progressed to BLx therapy.
- NBS combination therapy and BLx use, either as monotherapy or in combination with an NBS, increased in later lines of therapy.



- For patients who began on NBS therapy and progressed to BLx therapy, the mean (SD) time to BLx was 465 (302) days.

NBS=non-biologic systemic; BLx=biologic; NBS combo=NBS combination therapy; NBS/BLx combo=NBS and BLx combination therapy. *A patient was determined to have discontinued systemic therapy if his or her last observed systemic therapy claim expired prior to 180 days before the end of the look-forward period.

NBS Persistence Results



- Persistence to NBS therapy was poor, with averages of 29% and 12% at 12 and 36 months, respectively.

Canadian Retrospective Study

NBS Persistence Results

Variable	Outcome: Days to Discontinuation					
	Descriptive Statistics			Cox Proportional Hazards		
	N	%	Median Time to Discontinue	Hazard Ratio	95% CI	*P*
Total Sample	4,526	100	153.0			
Index Medication						
Methotrexate	2,024	44.7	181.5	1.00	Reference Group	
Acitretin	1,750	38.7	123.5	1.39	(1.29-1.49)	<0.0001
Hydroxychloroquine	314	6.9	184.0	0.88	(0.77-1.01)	0.059
Sulfasalazine	219	4.8	130.0	1.12	(0.96-1.30)	0.141
Azathioprine	118	2.6	209.0	0.89	(0.72-1.11)	0.307
Cyclosporine	60	1.3	125.5	1.34	(1.03-1.74)	0.032
Leflunomide	41	0.9	282.0	0.80	(0.57-1.12)	0.190
Gender						
Male	2,229	49.2	148.0	1.00	Reference Group	
Female	2,297	50.8	158.0	0.99	(0.93-1.06)	0.830
Age Group						
<40	689	15.2	151.0	1.09	(0.99-1.20)	0.068
40-64	2,694	59.5	154.0	1.00	Reference Group	
≥65	1,143	25.3	149.0	1.08	(0.98-1.20)	0.136
Patient Contribution*						
High	352	7.8	106.5	1.24	(1.08-1.41)	0.002
Medium	2,451	54.2	165.0	0.97	(0.89-1.05)	0.440
Low	868	19.2	166.0	1.00	Reference Group	
Unknown	855	18.9	127.0	1.14	(1.03-1.27)	0.014
Preexisting Comorbid Condition§						
Gastrointestinal	178	3.9	166.0	0.92	(0.77-1.09)	0.349
Diabetes	522	11.5	160.0	0.91	(0.82-1.01)	0.089
Cardiovascular	2,088	46.1	161.0	0.88	(0.82-0.95)	0.001
Anti-infective	1,212	26.8	147.0	1.11	(1.03-1.19)	0.005
Antidepressant	848	18.7	151.5	1.03	(0.95-1.12)	0.462
Respiratory	532	11.8	152.0	0.96	(0.87-1.06)	0.437

- The results of Cox proportional hazards modeling suggested preexisting *cardiovascular disease* was associated with ***better*** persistence, whereas treatment with *acitretin* or *cyclosporine*, having *high contribution levels* and having preexisting *anti-infective medications* were associated with ***poorer*** persistence.

Note: The patient's type of insurance plan (private vs. public) was controlled for in the models with private as the reference group (HR 0.92, *P*=0.056).

*The average patient contribution per day of therapy including patient copayments, deductibles, and other out-of-pocket expenses.
High ≥$1.00, Medium >$0.10 to <$1.00, Low ≤ $0.10/day of therapy.
§Comorbidity presence was measured based on indication-specific medication use within the washout period. Interpreted as the risk/odds of having the outcome in patients who had that medication class in comparison to patients who did not have that medication class in the washout period.
CI=confidence interval; HR=hazard ratio.

NBS Adherence Results

Variable	Outcome: Non-Adherence Over 36 Months — Descriptive Statistics N	%	% of pts with MPR <80	Logistic Regression — Odds Ratio	95% CI	*P*
Total Sample	3,796	100	80.5			
Index Medication						
Methotrexate	1,763	46.4	77.3	1.00	Reference Group	
Acitretin	1,430	37.7	87.7	2.14	(1.75-2.61)	0<.0001
Hydroxychloroquine	260	6.8	67.3	0.67	(0.50-0.89)	0.007
Sulfasalazine	169	4.5	78.1	1.06	(0.72-1.56)	0.771
Azathioprine	88	2.3	67.0	0.62	(0.38-1.01)	0.053
Cyclosporine	50	1.3	94.0	2.91	(0.89-9.59)	0.078
Leflunomide	36	0.9	72.2	0.81	(0.37-1.70)	0.553
Gender:						
Male	1,867	49.2	81.7	1.00	Reference Group	
Female	1,929	50.8	79.3	0.93	(0.79-1.10)	0.421
Age Group						
<40	585	15.4	85.6	1.41	(1.08-1.84)	0.012
40-64	2,254	59.4	80.6	1.00	Reference Group	
65+	957	25.2	77.1	1.06	(0.83-1.35)	0.631
Patient Contribution*						
High	277	7.3	93.1	2.80	(1.68-4.67)	<.0001
Medium	2,106	55.5	78.9	1.12	(0.91-1.38)	0.296
Low	767	20.2	76.4	1.00	Reference Group	
Unknown	646	17.0	85.3	1.56	(1.16-2.09)	0.003
Preexisting Comorbid Condition§						
Gastrointestinal	150	4.0	74.0	0.82	(0.54-1.23)	0.330
Diabetes	442	11.6	73.5	0.76	(0.59-0.97)	0.030
Cardiovascular	1,758	46.3	76.7	0.74	(0.61-0.90)	0.002
Anti-infective	1,018	26.8	81.4	1.22	(1.01-1.48)	0.043
Antidepressant	728	19.2	79.7	1.05	(0.85-1.31)	0.636
Respiratory	446	11.7	76.5	0.87	(0.67-1.11)	0.260

- For patients eligible for the adherence analysis (n=3,796), **81%** were non-adherent to their NBS over 36 months.
- Logistic regression analysis suggested treatment with *hydroxychloroquine* and preexisting *diabetes* or *cardiovascular dise*ase were associated with ***better*** adherence, whereas treatment with *acitretin*, being *under 40 years* of age, having *high patient contribution* levels and having preexisting *anti-infective medications* were associated with ***poorer*** adherence.

Note: The patient's type of insurance plan (private vs. public) was controlled for in the models with private as the reference group (OR 0.81, *P*= 0.06)

*The average patient contribution per day of therapy including patient copayments, deductibles, and other out-of-pocket expenses.
High ≥$1.00, Medium >$0.10 to <$1.00, Low ≤ $0.10/day of therapy.
§Comorbidity presence was measured based on indication-specific medication use within the washout period. Interpreted as the risk/odds of having the outcome in patients who had that medication class in comparison to patients who did not have that medication class in the washout period.

BLx Persistence and Adherence Results

Persistence

- Average persistence to BLx therapy (n=1,539) was 62% and 31% at 12 and 36 months, respectively.
- Cox proportional hazards modeling suggested:
  - Preexisting *gastrointestinal disease* (HR=0.68, *P*=0.004) was associated with **better** persistence.
  - *Females* (HR=1.21, *P*=0.002) and preexisting *respiratory disease* (HR=1.33, *P*=0.005) were associated with **poorer** persistence.

Adherence

- For patients eligible for the adherence analysis (n=1,485), 55% were non-adherent to their BLx over 36 months.
- Logistic regression analysis suggested:
  - Treatment with *ustekinumab* (OR=0.44, *P*<0.001) was associated with **better** adherence.
  - *Females* (OR=1.32, *P*=0.01) and preexisting *respiratory disease* (OR=1.63, *P*=0.01) were associated with **poorer** adherence.

OR=odds ratio.

Conclusion and Limitations

Conclusion

- In Canada, half of all psoriasis patients who commence a systemic drug therapy completely stop any systemic drug therapy within 3 years.
- In addition, persistence and adherence to initial systemic psoriasis therapy is poor, especially with conventional NBS drugs.
- Thus, a need for novel psoriasis treatment strategies exists.

Limitations

- The studied databases do not provide diagnosis code information; therefore, psoriasis patients were identified based on medication use. Similarly, comorbidities were determined based on medication claims.
- Patient contribution does not capture financial support provided by BLx manufacturers, which may contribute to the absence of an observed relationship between this covariate and persistence/adherence.

Appendix: Molecules for Patient Selection

Molecules Used to Select Patients at Various Stages of the Study

Psoriasis-Defining Molecules*	NBS Molecules	BLx Molecules
Acitretin	Acitretin	Abatacept
Calcipotriene	Azathioprine	Adalimumab
Calcipotriene + Betamethasone	Cyclosporine	Alefacept§
Calcitriol	Hydroxychloroquine	Anakinra
Methoxsalen	Leflunomide	Certolizumab Pegol
Trioxsalen	Methotrexate	Efalizumab§
	Sulfasalazine	Etanercept
		Golimumab
		Infliximab
		Rituximab
		Tocilizumab
		Ustekinumab

*Psoriasis-defining molecules are based on a previously published algorithm (Dobson-Belaire, et al. *Value Health*. 2014;17(7):A580 [Abstract]).

§Alefacept and efalizumab only included in the treatment progression analysis.