

Etanercept Patient Assistance Program: Another Data Source for Epidemiological Studies?

Brian C Chan¹, Soo Jin Seung¹, David McLean², Mary Bell³, Neil H Shear⁴ and Nicole Mittmann^{1*}

¹Health Outcomes and Pharmacoeconomics (HOPE) Research Centre, Division of Clinical Pharmacology, Sunnybrook Health Sciences Centre, Canada

²Adjuvantz, A Division of World Travel Protection Canada Inc

³Division of Rheumatology, Department of Medicine, Sunnybrook Health Sciences Centre, Canada

⁴Division of Dermatology, Department of Medicine, Sunnybrook Health Sciences Centre, Canada

Abstract

Background: Patient assistance programs (PAP) have been established for biologic disease modifying therapies such as etanercept to improve patient knowledge and compliance and provide a means for follow-up. The information collected through these programs is a potential data source to determine patient characteristics, patient outcomes, treatment adherence and reimbursement practices of individuals prescribed biologic disease modifying therapies.

Objective: To describe the population enrolled in the Enliven[®] Services Patient Assistance Program and to determine one-year retention rates.

Methods: A retrospective review of a Canadian cohort of patients enrolled in an etanercept PAP diagnosed with rheumatoid arthritis (RA) was conducted. Demographic and utilization information was collected for all subjects enrolled in the period between 2000 and 2007. One-year retention rates were also calculated from the data collected. Descriptive statistics were used to characterize the data.

Results: 14,335 subjects prescribed etanercept were enrolled in Enliven[®]. Average age at time of enrollment was 53 years. Three-quarters of subjects were female and four-fifths were English speaking. The largest percentage of individuals resided in Ontario and Quebec. The retention rate at one year for etanercept therapy was 82%.

Conclusion: The analysis provides a snapshot of individuals administered etanercept therapy over a 7-year timeframe. PAPs can be a valuable source of data for research on biological therapies in addition to the support provided to the patients.

Keywords: Patient assistance program; Biological therapy; Rheumatoid arthritis

Abbreviations: LDL: Low-density Lipoprotein; PAP: Patient Assistance Program; RA: Rheumatoid Arthritis; US: United States

Introduction

For individuals with chronic diseases such as rheumatoid arthritis (RA), medication adherence is associated with a patient's personal belief that taking medication as prescribed results in optimal benefit and ease with self-administering the medication [1]. Thus, patient assistance programs (PAPs) have been established to enhance access to therapies, provide information on the disease and treatment, collect information on adverse events and provide information on the administration of the drug.

The information collected through PAPs represents an untapped source of clinical information that can be utilized to generate information on patient characteristics, patient outcomes, treatment adherence and reimbursement practices. Several studies have investigated patient outcomes with enrollment into PAPs [2-7]. Other reports of biologic PAPs for RA have presented dosing patterns [8].

In Canada, the Enliven[®] Services Patient Assistance Program, is a PAP for etanercept, a biologic disease modifying agent. Since etanercept is a self-injection therapy, there is a need for patient education and support. In Canada, the Enliven[®] Services Patient Assistance Program was established in 2000 to provide self-injection training; patient support through a toll-free telephone line; a mechanism to report adverse events; and guidance to navigate through reimbursement

coverage options. Individuals prescribed etanercept are informed of the Enliven[®] program through their physician, pharmacist or The Arthritis Society. Enliven[®] provides regular and consistent contact with patients and families who have been diagnosed with conditions such as rheumatoid arthritis (RA), psoriasis, psoriatic arthritis, ankylosing spondylitis and juvenile rheumatoid arthritis, through scheduled telephone contact several times in the first year, followed by annual calls.

This PAP has not been comprehensively analyzed and as such there is an opportunity to leverage this information on a cohort of real world patients and utilization of etanercept at a national level. This study will present and describe the data that is currently available from a specific PAP.

Objectives

The objectives of this study were to describe the population enrolled

***Corresponding author:** Nicole Mittmann, Executive Director, HOPE Research Centre, Scientist, Sunnybrook Health Sciences Centre, Assistant Professor, Department of Pharmacology, University of Toronto, 2075 Bayview Avenue, E240, Toronto, Ontario M4N 3M5, Canada, Tel: 416-480-6100 ext. 1652; Fax: 416-480-6025; E-mail: nicole.mittmann@sri.utoronto.ca

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in the Enliven® Services PAP (e.g., demographics, indication, location of drug training) and to examine one-year retention rates.

Methods

This study is a retrospective review of the data collected in a PAP database. Specifically, PAP enrollment population characteristics and estimate the one-year retention rate will be presented.

For this analysis, only the individuals with RA were included. The timeframe for the de-identified and anonymized longitudinal dataset was from June 2000 to December 2007. Consent from individuals was collected upon enrollment into Enliven®.

Information on age, gender, language, residence, indication, training location, timing of treatment, and delays in treatment details were reviewed. Retention was defined as treatment continuation at one year from etanercept therapy start date. Confirmation of treatment retention at one year was based on contact between the PAP and subjects receiving a follow-up call scheduled to occur one year after enrollment. For subjects who were not successfully contacted at the scheduled follow-up call, treatment retention at one year was assumed if there was a recorded provincial or private insurance start or stop date for drug cost reimbursement beyond one year of the therapy start date or if they indicated that they were still on the drug beyond the one year scheduled follow-up call. Individuals without information at the confirmed follow-up call or those who did not have recorded dates for provincial or private insurance drug cost coverage beyond one year of therapy start date were excluded from the analysis.

Demographic data was collected for all subjects enrolled including individuals who declined telephone follow-up calls from the Enliven® program during the first year of etanercept treatment. Individuals contacting the Enliven® program had the option of declining telephone follow-up, but remain in the PAP for the other services that Enliven® provided. Descriptive statistics (mean, standard deviations) were used to characterize the information collected. Data was stratified by whether the subject accepted follow-up telephone calls from the Enliven® program or declined follow-up calls.

A comparison of subject characteristics between individuals accepting follow-up calls and individuals declining follow-up calls was also conducted.

Results

A total of 14,335 RA subjects were enrolled in Enliven® between June 7, 2000 and December 28, 2007. Table 1 summarizes the characteristics for the entire cohort.

Of the total RA cohort, follow-up information was available for 13,953 (97%) individuals enrolled. Of the cohort where follow-up information was available, 79% had retention data (Table 2). Eighty-two percent of the Enliven® cohort indicated that they were still using and administering etanercept at one year post-Enliven® enrollment.

Discussion

The Enliven® program, along with other PAPs, may offer an important data source for characterizing utilization and administration of treatments in the real world. Although not established for research purposes, they may offer an opportunity for follow-up care management post prescription of a medication.

It is also important to highlight that this is the first study of retention rates based on a large Canadian PAP cohort who were administered

Table 1: Characteristics for the entire Enliven® cohort.

Variable	Entire cohort	Enliven enrollees consenting to follow-up calls	Enliven enrollees declining follow-up calls
Sample size (% of entire cohort)	14,335 (100%)	13,953 (97.3%)	382 (2.7%)
Mean age of the population (± SD)	52.5 ± 14.9 years	52.6 ± 14.8 years	50.3 ± 17.0 years
Number who are etanercept naïve	13,716 (95.7%)	13,339 (95.6%)	377 (98.7%)
Number of females	10,589 (73.9%)	10,332 (74.0%)	257 (67.3%)
Primary language of communication, n (%)			
English	11,374 (79.3%)	11,036 (79.1%)	338 (88.5%)
French	2,948 (20.6%)	2,904 (20.8%)	44 (11.5%)
Province of residence, n (%)			
Ontario	6,088 (42.5%)	5,922 (42.4%)	166 (43.5%)
Quebec	3,178 (22.2%)	3,125 (22.4%)	53 (13.9%)
British Columbia	1,657 (11.6%)	1,596 (11.4%)	61 (16.0%)
Alberta	1,308 (9.1%)	1,261 (9.0%)	47 (12.3%)
Nova Scotia	576 (4.0%)	562 (4.0%)	14 (3.7%)
New Brunswick	416 (2.9%)	412 (3.0%)	4 (1.0%)
Manitoba	442 (3.1%)	427 (3.0%)	15 (3.9%)
Saskatchewan	399 (2.8%)	382 (2.7%)	17 (4.4%)
Newfoundland	209 (1.5%)	205 (1.5%)	4 (1.0%)
Prince Edward Island	45 (0.3%)	44 (0.3%)	1 (0.2%)
North West Territories	12 (0.1%)	12 (0.1%)	0
Yukon Territories	3 (<0.1%)	3 (<0.1%)	0
Nunavut	2 (<0.1%)	2 (<0.1%)	0
Location of drug administration and who administered n (%)			
Patient's home	4,326 (30.2%)	4,292 (30.8%)	34 (8.9%)
Rheumatologist office	2,725 (19.0%)	2,605 (18.7%)	120 (3.1%)
Medical clinic	2,104 (14.7%)	2,047 (14.6%)	57 (14.9%)
General Practitioner's office	1,292 (9.0%)	1,262 (9.0%)	30 (7.9%)
Person who administered, n (%)			
Previously trained (old patient)	1,449 (10.1%)	1,404 (10.1%)	45 (11.8%)
None	683 (4.8%)	637 (4.6%)	46 (12.0%)
Self	564 (3.9%)	546 (3.9%)	18 (4.7%)
Nurse	476 (3.2%)	465 (3.2%)	11 (2.9%)
To be determined	396 (2.8%)	383 (2.7%)	13 (3.4%)
Other	319 (2.2%)	311 (2.2%)	8 (2.0%)
Spouse	1 (<0.1%)	1 (<0.1%)	0

Table 2: Subgroup cohort sample sizes.

Subgroup	Total
Total subgroup enrolled in Enliven® with Rheumatoid Arthritis	14,335
Total with follow-up information after enrollment	13,953
Cohort with less than 1-year follow-up	2,462
Cohort with complete retention data	10,985

a biologic treatment. Our results showed that 82% of individuals who received etanercept remained on the treatment at one year after initiating treatment. This observation was found to be at the higher end of a recent review of adherence rates for biologic treatments in an RA population [9]. In that review, 12-month adherence values ranged from 42% to 89%. The authors of that review noted that adherence definitions and data sources varied widely between the different studies and discouraged comparison of adherence values. Of note, another review of etanercept adherence (reported as persistence in that publication)

observed rates at one-year ranged between 69% to 87% based on four studies [10].

Specific to this study, results showed that individuals enrolled in this program were on average 53 years of age, predominantly female and English speaking. Most individuals were from Ontario and Quebec. Approximately one-third of individuals received drug administration training from home.

Two studies have analyzed treatment adherence associated with PAP. A recent prospective cohort US study analyzed adherence to mesalamine in ulcerative colitis patients enrolled in a nurse-delivered PAP compared to standard care (physician follow-up) [4]. The results from that analysis did not show an improvement in mesalamine adherence or quality of life for individuals in the PAP. The authors concluded that discussing the concept of adherence as well as informing the individual that they will be monitored was enough to improve adherence. This conclusion suggests that the results of this study should be viewed with caution and highlights the inherent bias of prospective studies due to the required informed consent of participating individuals. Clinical trials that have been completed regarding PAP but unpublished thus far include a study of PegIntron Pen/Rebetol adherence in Hepatitis C individuals with a PAP (which includes additional medications for prophylaxis and treatment, psychotherapy, patient support groups, other health care professional support and educational literature) [11]. The number of participants who complete treatment at 24 or 48 weeks has not been presented yet. However, preliminary results present the mean (\pm standard deviation) length of treatment with PegIntron/Rebetol and PAP as 27.3 (\pm 14.7) compared to 28.8 (\pm 14.6) without PAP.

Additional studies are currently ongoing looking at the impact of PAP to disease state and treatment adherence in individuals with early stage breast cancer, with elevated LDL-cholesterol and taking atorvastatin [12,13].

There are several limitations to our study. One of the main limitations of PAPs is the lack of a comparative group. Typically PAPs have only focused on utilization for a specific treatment. Comparative PAPs amongst drugs in the same classes may provide information on the differential effects between medications. Future studies comparing the PAP data of similar treatments would provide invaluable information regarding the differences in retention rates, characteristics of treatment subjects and reasons for treatment delays between treatments. This information will help inform physicians who administer biologic therapies resulting in better care for patients. It is important to note that individuals are connected with the Enliven[®] program through their physician or nurse and that individuals declining registration are not reported to Enliven[®] thus, the significance of this cohort is unknown. As well, the information collected by Enliven[®] was based on enrollee's self-reports. Thus the accuracy of the results was dependent on the accuracy of the information reported. For instance, the retention rate was dependent on the accuracy of recorded dates of provincial or private insurance drug cost coverage. Also, a maximum of five follow-up telephone calls were issued to each consenting enrollee in the Enliven[®] program. Not all enrollees could be reached, although several follow-up calls were placed for each unsuccessful attempt at contact. Individuals who could not be contacted one year post therapy start date, and did not have start or stop dates for reimbursement post-one year were not considered retained at one year. However, there is a possibility that some of these individuals continued to remain on etanercept treatment and were lost to follow-up. As well, gaps in drug administration could not be accurately identified for individuals who were not successfully

reached at every telephone call. Data such as disease severity and safety outcomes were not included in our analyses. Finally the Enliven[®] cohort was based on a Canadian population, thus the applicability of the results presented are limited to a Canadian population.

Information on the utilization of medications in the community is not systematically collected. However, PAPs are becoming increasingly more prevalent in drugs new to the Canadian market. Provincial decision making bodies may ask for "value added" programs related to new formulary additions and PAPs have been used to describe patient populations and measure clinical or financial outcomes.

It is our hope that this study is the first in a series of research studies that will examine usual care through an already existing PAP mechanism for subjects receiving different classes of medications in the community. Though not meant to be a replacement for administrative data, PAP data may be able to address some of the limitations of other data sources. Drug claims data rely on prescription fills as a surrogate for prescription drug use. PAP on the other hand collects patient reported drug use. Also, by providing value added programs to patients, PAP may encourage better long-term follow-up compared to traditional cohort studies. PAPs provide another means for collecting long-term data on a large cohort of patients. Additional studies need to be conducted comparing the different data collection sources to characterize the strengths and weaknesses of the different methods.

We ask that researchers and clinicians leverage these programs to not only follow subjects prospectively for administrative purposes but that these existing infrastructures be adapted to collect information relevant to both patients and decisions makers. Relevant information including longitudinal examination of adverse events, complications, quality of life and outcomes related to treatments over time would provide a type of post-marketing surveillance not typically available. There is also an incentive for PAP administrators to collaborate with researchers and clinicians.

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