Improved Clinical Outcomes for Patients Receiving Immunoglobulin Therapy Through Specialty Pharmacy or Home Infusion Services

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Outline

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Disclosures

- This research was sponsored by Walgreens Co. and Option Care.
- Jordan Orange
  - Consulting – Walgreens/Optioncare, Baxalta, CSL Behring, ADMA biologics, Grifols, ASD healthcare
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[1.] Study oversight / management [2.] Clinical oversight [3.] Data management and statistical analysis

Learning Objectives

- Explore the implications of management in specific sites of care for application of therapeutic IG
- Consider opportunity for physician-pharmacist-nurse collaboration in “holistic” infusion patient management

Sites of care for provision of therapeutic Ig

Site of Care	Healthcare provider supervision	JACHO standards	Patient characteristics
Hospital Inpatient	Physician and Nurse	Yes	History of severe AE's Discomfort with below
Hospital Outpatient	Physician and Nurse	Yes	History of more than mild AE's. Discomfort with below
Physician Office	Physician or physician delegate and Nurse or nurse equivalent	Possibly	History of more than mild AE's Cognitive/physical limitations
Community Infusion center*	Nurse	Rarely	Mild or no AE's Management by antihistamines/analgesics
Home (Managed)	Nurse	No	Mild or no AE's
Home (Unmanaged)	Non-healthcare infusion partner	No	Minimal or no AE's

Based upon the AAAAI Ig Site of Care guidelines:
http://www.aaaai.org/Aaaai/media/MediaLibrary/PDF%20Documents/Practice%20Resources/Guidelines-for-the-site-of-care-for-administration-of-IGIV-therapy.pdf

*Site of care not listed in AAAAI guidelines

Knowledge gaps

- Are there bona fide advantages to specific sites of care?
  - Multiple studies point to improved QOL for SCIG at home, as well as some financial benefits seen in other countries.[1,2]
- Are there advantages to particular practice within sites of care?

[1]J. Clin Immunol 2012 32:1180-1192
[2]J. Clin Immunol 2008 28:370-8

IG clinical management: Alternate site care

In this study, the care models provide	Home Infusion	Specialty Pharmacy
Pre-infusion pharmacist evaluation for comorbidities affecting risk of ADR	IVIG/SCIG	SCIG
Individualized infusion plan	IVIG/SCIG	IVIG/SCIG
RN educates patient for self infusion	SCIG	SCIG
RN educates patient and clinically monitors infusion	IVIG	IVIG
Clinical follow up with patient and MD: adherence, ADR management and dose adjustment	IVIG/SCIG	IVIG/SCIG
Disease specific patient reported outcome measures communicated to MD	IVIG/SCIG	IVIG/SCIG
IG specialized RN, pharmacist, insurance team	IVIG/SCIG	IVIG/SCIG
Access to all IG products	IVIG/SCIG	IVIG/SCIG

Hypotheses

SCIG or IVIG patients who were managed by specialty pharmacy or IG-specialized home infusion have…

- Comparable/better clinical outcomes
  - Lower adverse event rates
  - Lower infection rates
- Lower costs

…compared to propensity-score matched patients across sites of care.

Study Design and Methods

- **Study Design:** Retrospective, cohort study using large administrative claims database (IMS Pharmetrics Plus)

- **Study Period:** September 1, 2011 to June 30, 2014

- **Statistical Methods:**
  - 1:4 propensity-score matching
  - Wilcoxon rank-sum test/Generalized Estimating Equation (GEE) models
  - Analyses were performed at patient-level using SAS 9.2

Note. Research approved by Quorum IRB (#28495/1).

Study Design and Methods

Variable Type	Variable
Clinical Outcomes	Adverse Events (IP, ER, OP)
	Infections (IP, ER, OP)
Economic Outcomes	Healthcare Costs (Total, IP, ER, OP, RX, IG)
Covariates	Administration route[1]
	Autoimmune Disease[1]
	Age at index date[2]
	Gender[2]
	Patients' Access to Center[2]
	Geographic Region[2]
	Charleson Comorbidity Index (CCI) [2]
	6-month Pre-Index Cost[2]
	Patient management status[3]
	Number of IG administrations (IVIG only)[3]
	Place of Service[3]
	Diabetes[3]
	Renal disease[3]

Notes. 1. Direct matched variable 2. Propensity-score matched variable 3. Other covariates;
Abbreviations: IP=inpatient, OP=outpatient; ER=emergency room RX=pharmacy; IG=immunoglobulin

Study Sample

Characteristics	P value before Matching		P value after matching			
			Propensity-Adjusted[1]		Propensity/Regression-Adjusted[2]	
	SCIG (Case N=89 Control N=831)	IVIG (Case N=306 Control N=4,429)	SCIG (Case N=59 Control N=236)	IVIG (Case N=227 Control N=908)	SCIG (Case N=45 Control N=180)	IVIG (Case N=242 Control N=968)
Age at index date (years)	0.3273	0.3366	0.7741	0.5834	0.4931	0.1119
Age Group	0.2457	0.0585	0.6757	0.9674	0.9472	0.6529
Gender at index	0.5943	0.7658	0.1905	0.9290	0.2888	0.9080
US Census Region	<.0001	<.0001	0.9632	0.7900	0.7446	0.9681
Patient Access to Center	0.0149	<.0001	0.6340	0.5416	0.9456	0.4649
Autoimmune disease (yes/no)	0.0099	0.8577	0.0789	0.5822	1.0000	1.0000
Pre_Total_Cost					0.3508	0.8277

…no differences after matching

1. See next slide for description of propensity vs. propensity regression-adjusted matching. 2. Degradation of sample size was due to additional criteria of 6-month pre-index costs for propensity match criteria.

Propensity versus. Propensity/Regression-adjusted matching

Propensity-adjusted: Cases were 1 to 4 propensity score matched to the control group on age group, gender, region, patient's access to center, autoimmune disease (yes/no), and CCI score.

Propensity/Regression-adjusted: Matching variables are the sample as above except adding 6-month pre-index cost. Regression models were further adjusted for covariates that were not included in the matching variables. The covariates are as listed below:

Cases vs. Controls (Clinical model)		Cases vs. Controls (Economic model)	
SCIG	**IVIG**	**SCIG**	**IVIG**
Patient Management Status	Patient Management Status	Patient Management Status	Patient Management Status
	Number of IG administrations		Place of Service*
	Place of Service*		Number of IG Administrations (IVIG only)
	Diabetes (yes/no)		
	Renal diseases (yes/no)		

*Place of service variable was categorized as:

1) Physician office
2) Hospital (hospital inpatient/outpatient)
3) Home infusion (all other POS including Home/Pharmacy/Other/Unknown, etc.)

Propensity-Adjusted Clinical Results

Clinical Outcomes	SCIG			IVIG		
	Cases	Controls	*P*	Cases	Controls	*P*
N	59	236		227	908	
Rate (events / patient / year)						
Infections						
All Infections	3.71	2.63	0.087	2.64	2.43	0.653
Serious Bacterial Infections	0.29	0.17	0.208	0.16	0.29	0.320
Other Infections	3.42	2.56	0.232	2.48	2.16	0.462
Adverse Events (AE)						
Common AE	N/A			0.02	0.03	0.550
Serious AE	**0.08**	**0.34**	**0.050**	0.01	0	0.150
Mild Less Common AE (Subjective)	**0.08**	**0.01**	**0.005**	0.03	0.04	0.350
Mild Less Common AE (Objective)	N/A			0.20	0.23	0.780
Proportion of Patients (% of patients)						
Infections						
All Infections	66.10	67.80	0.804	52.42	53.08	0.858
Serious Bacterial Infections	3.39	4.66	1.000	4.41	6.83	0.180
Other Infections	64.41	66.95	0.712	51.54	50.66	0.812
Adverse Events (AE)						
Common AE	N/A			1.76	2.75	0.397
Serious AE	5.08	9.75	0.259	1.32	0.44	0.147
Mild Less Common AE (Subjective)	**5.08**	**0.85**	**0.056**	2.20	3.85	0.227
Mild Less Common AE (Objective)	N/A			8.37	6.61	0.351

Propensity/Regression-Adjusted Clinical Results

Clinical Outcomes	SCIG			IVIG		
	Cases	Controls	*P*	Cases	Controls	*P*
N	45	180		242	968	
Rates (events / patient / year)						
Infections						
All Infections	3.46	4.40	0.463	2.71	2.06	0.274
Serious Bacterial Infections	0.02	0.15		**0.12**	**0.45**	**0.066**
Other Infections	3.41	4.25	0.509	2.52	1.85	0.241
Adverse Events (AE)						
Common AE	N/A			0.02	0.03	0.776
Serious AE	0.11	1.31		0.02	0.01	
Mild Less Common AE (Subjective)	0.09	0.00	0.333	0.04	0.03	0.333
Mild Less Common AE (Objective)				0.23	0.23	
Proportion of Patients (% of patients)						
Infections						
All Infections	66.67	70.00	0.665	54.13	53.20	0.795
Serious Bacterial Infections	2.22	3.89	1.000	**4.13**	**7.75**	**0.049**
Other Infections	66.67	69.44	0.719	52.89	50.31	0.472
Adverse Events (AE)						
Common AE	N/A			1.65	2.69	0.355
Serious AE	6.67	12.22	0.289	1.65	0.62	0.120
Mild Less Common AE (Subjective)	**4.44**	**0.00**	**0.039**	3.72	4.13	0.771
Mild Less Common AE (Objective)				9.92	7.23	0.163

*Rates in blue were *not* adjusted for additional covariates due to model convergence issues.

Propensity-Adjusted Economic Results

Total Allowable Costs (Mean Costs / Patient / Year, $)	SCIG				IVIG			
	Case	Control	*P*	Δ	Case	Control	*P*	Δ
N	59	236			227	908		
Total costs	75,030	75,545	0.881	515	112,756	120,567	0.285	7811
IG-related	47,302	52756	0.127	5,454	74,181	75,328	0.945	1148
Total inpatient costs	2,912	4,312	1.000	1,399	8,615	8,002	0.356	(612)
Total ER costs	**110**	**542**	**<.0001**	**432**	958	675	0.276	(284)
Total outpatient costs	33,151	34,921	0.832	1,770	96,936	104,049	0.264	7113
IG-related	**15,964**	**22,752**	**0.050**	**6,788**	73,969	74,773	0.912	804
Total pharmacy costs	38,856	35,770	0.985	(3,086)	**6,247**	**7,841**	**0.041**	**1,594**
IG-related	31,338	29,927	0.769	(1,411)	0	471	NA	471

Propensity/Regression-Adjusted Economic Results

Total Allowable Costs Mean Costs / Patient / Year ($)	SCIG				IVIG			
	Case	Control	*P*	Δ	Case	Control	*P*	Δ
N	45	180			242	968		
Total costs	66,450	87,318	0.009	20,868	109,476	135,998	0.002	26,522
IG-related	48,248	58,834	0.168	10,586	64,332	81,827	0.001	17,495
Total inpatient costs	3,398	11,347	0.030	7,949	8,781	14,137	0.236	5,356
Total ER costs	222	344	0.435	122	992	482	0.107	(510)
Total outpatient costs	28,008	49,325	0.0003	21,317	93,865	108,561	0.026	14,696
IG-related	16,650	40,059	0.001	23,409	64,080	81,349	0.001	17,269
Total pharmacy costs	26,543	34,353	0.398	7,810	6,666	8,183	0.189	1,517
IG-related	27,887	23,507	0.522	(4,380)				

Limitations

- **Sample Size:** The power of the analysis was limited by sample size.

- **As with all match studies, the following limitations apply:**
  - Matching is not perfect even when all possible variables are available.
  - Some confounding variables are not available in administrative data.

Conclusions

Specialized home infusion/pharmacy services of Ig is associated with:

- Lower SAE rates for SCIG (hypothesis confirmed)
- Higher reported mild AE rates for SCIG (unexpected)
  - Perhaps reporting bias
- Lower SBI rates for IVIG (near significance - unexpected)
- Lower overall costs for both SCIG and IVIG (unexpected)
  - Mostly reflected in outpatient costs