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VALUE IN HEALTH

Cost Savings from Intravenous Immunoglobulin Manufactured from Chromotography/Caprylate (IGIV-C) in Persons with Primary Humoral Immunodeficiency Disorder

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ABSTRACT

Objective: Human intravenous immunoglobulin manufactured with chromatography and caprylate methods (IGIV-C, 10%) was associated with a reduction in validated infections (pneumonia and sinusitis) compared with treatment with a licensed immunoglobulin product manufactured using standard solvent-detergent methods (IGIV-SD™, 10%) in participants with primary humoral immunodeficiency disorder (PIDD). Our objective was to determine the cost-consequences of using IGIV-C instead of IGIV-SD.

Methods: Economic analysis of a double-blind, randomized, clinical trial was used. Participants were randomly assigned to IGIV-C (N = 87) or IGIV-SD (N = 85) and monitored for the development of validated infections over the course of 9 months. Consumed resources were enumerated including cost of physician and emergency room visits, medications (prescription and over-the-counter), work productivity losses, and hospitalizations. Resource data was obtained from case report forms, patient diaries and the trial medication database. Because the amount of IGIV-SD used exceeded that of IGIV-C (nonstatistically significant difference) and the products are equivalently priced, we conservatively excluded investigational product acquisition cost to avoid artificially biasing incremental cost differences. We used a societal perspective with indirect costs, measured in 2003 US dollars. Pricing of both IGIV products is anticipated to be equivalent.

Results: In a multivariate analysis, annual mean per participant costs were significantly lower between those receiving IGIV-C compared with IGIV-SD for prescription medications [–$302, 95% confidence interval (CI) –$598 to –$6], hospitalization (–$1454, 95% CI –$1828 to –$1080) and total costs (–$1304, 95% CI –$1867 to –$742). Costs associated with lost work productivity and physician visits were similar in both groups ($P > 0.10$). In sensitivity analyses, varying costs of concomitant medications, hospitalization and outpatient care, did not significantly change our results.

Conclusion: IGIV-C is cost-saving compared with IGIV-SD among persons with PIDD.

Keywords: economics, immunoglobulin, manufacturing, primary immune deficiency, sinusitis.

Introduction

Polyvalent intravenous IgG (IGIV) is manufactured from human plasma, pooled from thousands of donors and used to treat a variety of approved and off-label conditions such as primary humoral immunodeficiency disorder (PIDD), idiopathic thrombocytopenic purpura, multiple sclerosis, chronic inflammatory demyelinating polyneuropathies, bullous skin diseases and many others [1]. To create the perfect therapeutic IGIV solution, manufacturing processes need to maintain the integrity and biologic activity of each IgG molecule, while simultaneously removing unwanted viruses, prions and other pathogens. Refinements in manufacturing over the years have led to third-generation IGIV products many of which use solvent/detergent (SD) methods for improving the safety of plasma-derived products and isolation of IgG [2,3]. Nevertheless, SD methods can alter immunoglobulin yield and function [4].

Recently, the US Food and Drug Administration approved a new IGIV product (IGIV-C, 10%, Gamunex®, Bayer Health Care, Biological Products

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Table 1 Demographic characteristics of primary humoral immunodeficiency participants enrolled in clinical trial on an intent-to-treat basis

	IGIV-C (n = 87)	IGIV-SD (n = 85)
Age, mean ± SD	34.9 ± 20.5	29.8 ± 18.3
Sex, n (%) men	60 (69)	49 (58)
Ethnicity, n (%) white	75 (86)	71 (84)
Weight (kg), mean ± SD	66.4 ± 25.7	61.3 ± 26.4
Height (cm), mean ± SD	162.4 ± 22.8	158.7 ± 23.3
Pre-existing bronchiectasis, n (%) with	17 (20)	18 (21)
3-week dosing schedule for IV, n (%) with	10 (11)	18 (21)
Previous IGIV dose (mg/kg), mean ± SD	432.7 ± 122.6	454.6 ± 125.1
Duration of follow-up in trial, days ± SD	256.7 ± 66.0	266 ± 53.3
Total number of baseline prescriptions	308	307

None of the above differences were statistically significant.

Division, LLC., Research Triangle Park, NC) that is manufactured with an entirely new process using large scale chromatography and caprylate techniques (for purification and viral inactivation). Compared with an IGIV manufactured from SD methods (Gamimune N™, also Bayer Health Care, IGIV-SD, 10%), IGIV-C demonstrated increased IGIV yield from plasma, more rapid viral inactivation kinetics and an improved physiological IgG subclass distribution (specifically higher IgG4 levels) [4–6]. Moreover, in a randomized, double-blind, head-to-head clinical trial among patients with PIDD, IGIV-C was associated with a reduction in the percentage of PIDD patients with at least one validated sinopulmonary infection, translating into a statistically significant decrease in annualized infection rate compared with IGIV-SD [7].

Primary humoral immunodeficiency disorder patients typically require lifelong, periodic, replacement therapy with IGIV to prevent infections from encapsulated bacteria. The standard of care for PIDD patients is IGIV infusions every 3 to 4 weeks, generally between 300 and 600 mg/kg [8] and the annual per patient costs are high [9]. Although there is support for the clinical advantages seen in PIDD, the cost consequences of using the new IGIV-C product has not been investigated.

To better understand the economic impact of using differently manufactured IGIV products, we examined the cost consequences of using IGIV-C compared with IGIV-SD in patients with PIDD. Given the high morbidity and costs associated with sinopulmonary infections commonly associated with PIDD, payers and providers should choose a treatment strategy that maximizes value.

Methods

Study Design

We conducted a retrospective economic analysis of the randomized controlled trial comparing the efficacy and safety of IGIV-C versus IGIV-SD in the treatment of PIDD. A complete description of the clinical trial has been previously published [7]. Briefly, the trial was conducted at 25 centers in the United States and Canada from March 8, 1999 to June 19, 2000. A total of 172 participants were enrolled (87 were assigned to IGIV-C; 85 to IGIV-SD). All participants had a confirmed diagnosis of PIDD as defined by World Health Organization (WHO) criteria, including but not limited to congenital agammaglobulinemia or hypogammaglobulinemia including X-linked and autosomal forms, common variable immunodeficiency, severe combined immunodeficiency, and Wiskott–Aldrich syndrome. The participants were followed for 9 months from the day of first infusion. Tables 1 and 2 summarize data from the clinical trial. Demographic differences were not statistically significant.

Table 2 Efficacy analysis of IGIV-C compared with IGIV-SD, 10%

	IGIV-C (n = 73)	IGIV-SD (n = 73)	*P* value
Validated infections*	9 (12%)	17 (23%)	$P = 0.06$
Pneumonia	0	2 (3%)	NS
Acute sinusitis	4 (5%)	10 (14%)	$P = 0.09$
Acute exacerbation of chronic sinusitis	5 (7%)	6 (8%)	NS
Annualized validated infection rate (per 100 person-years)	18	43	$P < 0.05$

*Validated infections are pneumonia, acute sinusitis and acute exacerbation of chronic sinusitis.
NS, not statistically significant $P > 0.1$.