Pharmacoeconomic Analysis of a Unique Immune Globulin Containing a Blend Of High-Titer RSV and Normal Source Plasma Compared With IVIG+palivizumab in a Patient With SCID

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Disclosures

- Jeffrey Gruenglas, Co-author. ADMA Biologics, Ramsey, NJ
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SCID Patient Journey and Clinical Challenges

Severe Combined Immunodeficiency

- Inherited primary immunodeficiency disorder characterized by profound cellular and humoral immune defects[1]
- Relatively rare disorder[2]
  - ~100 cases/year in US
- Newborn screening (NBS) has revolutionized how we identify these patients soon after birth[1,3]
  - However, NBS has not eliminated some of the clinical challenges that remain

NBS=newborn screening; SCID=severe combined immunodeficiency.

1. American Academy of Allergy, Asthma & Immunology website. https://www.aaaai.org/Conditions-Treatments/primary-immunodeficiency-disease/severe-combined-immunodeficiency. Accessed June 2, 2021.
2. National Human Genome Research Institute website. https://www.genome.gov/Genetic-Disorders/Severe-Combined-Immunodeficiency. Accessed June 2, 2021. 3. van der Burg M, et al. *Front Pediatr*. 2019;7:373.

How Do Patients Present?

- SCID babies typically appear normal at birth[1]
- May present with recurrent infections, chronic diarrhea, and failure to thrive[1]
- Highest risk for severe, life-threatening infections occur after the waning of transplacentally acquired maternal antibody[1]
- SCID was the first primary immune-deficiency disease that was amenable to NBS and currently has been adopted in all 50 states[1]
  - Avoidance of severe and fatal infections was the impetus[2]

NBS=newborn screening; SCID=severe combined immunodeficiency.

1. Seth D, et al. *Clin Pediatr.* 2019;58(10):1124-1127. 2. Dorsey MJ, *J Allergy Clin Immunol*. 2017;139(3):733-742.

Management of SCID: Immunologic Emergency

Definitive treatment

- Hematopoietic stem cell transplant (HSCT)
- Gene therapy (ADA, XL-SCID)

Other treatment modalities

- Enzyme replacement therapy (PEG-ADA)

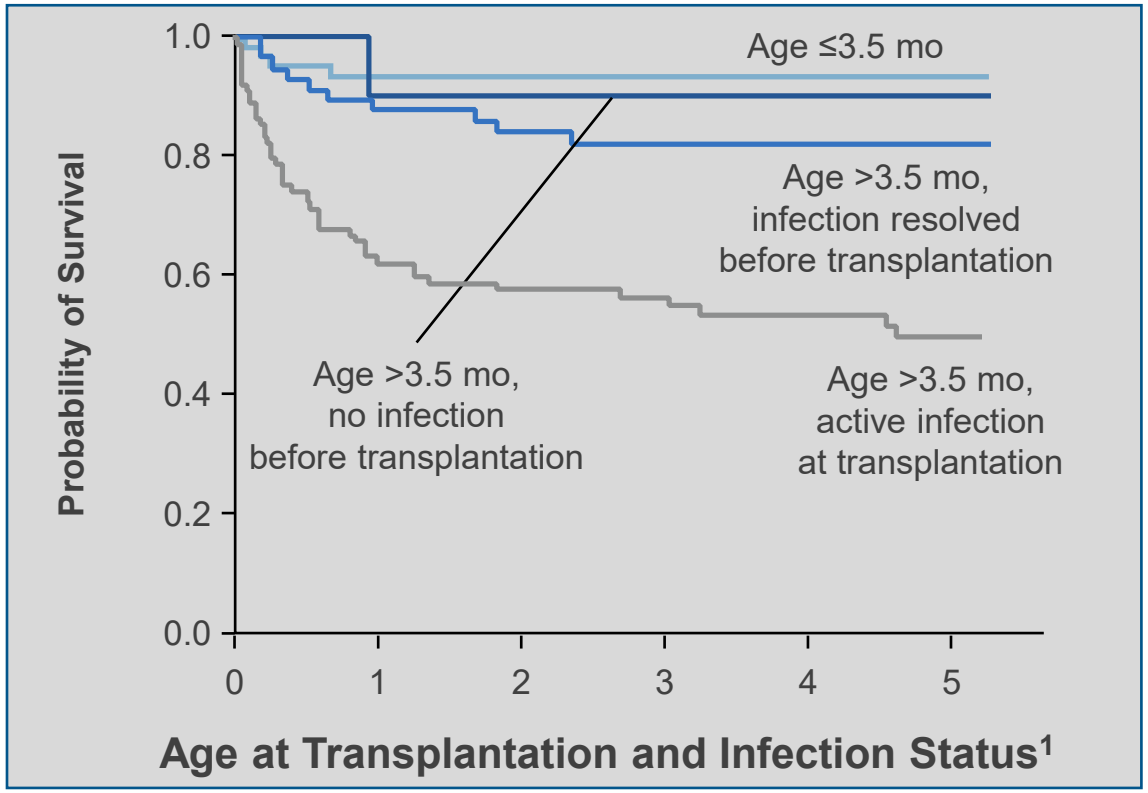
Adjuvant therapies/ practice

- IVIG
- Prophylactic anti-infectives
- CMV negative blood products
- Irradiated blood products
- Protective isolation

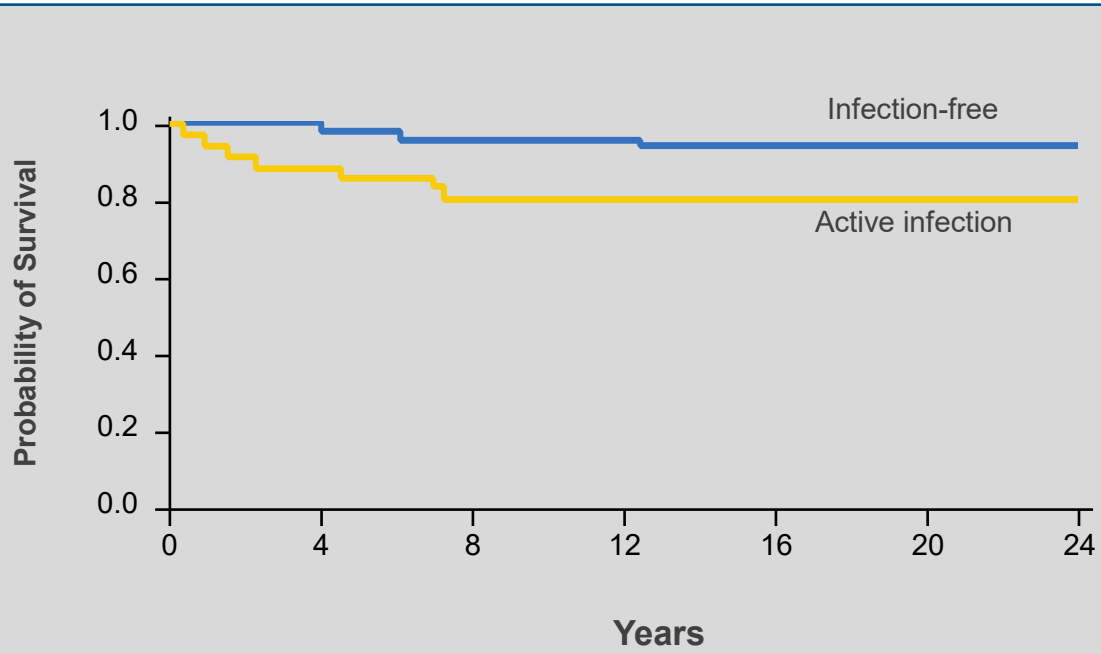
ADA=adenosine deaminase; CMV=cytomegalovirus; HSCT=hematopoietic stem cell transplant; IVIG=intravenous immune globulin; PEG-ADA=polyethylene glycol-modified adenosine deaminase.

HSCT Outcomes in Infants with SCID

Time to transplant and infection correlates with poor survival and outcomes



Age at Transplantation and Infection Status[1]



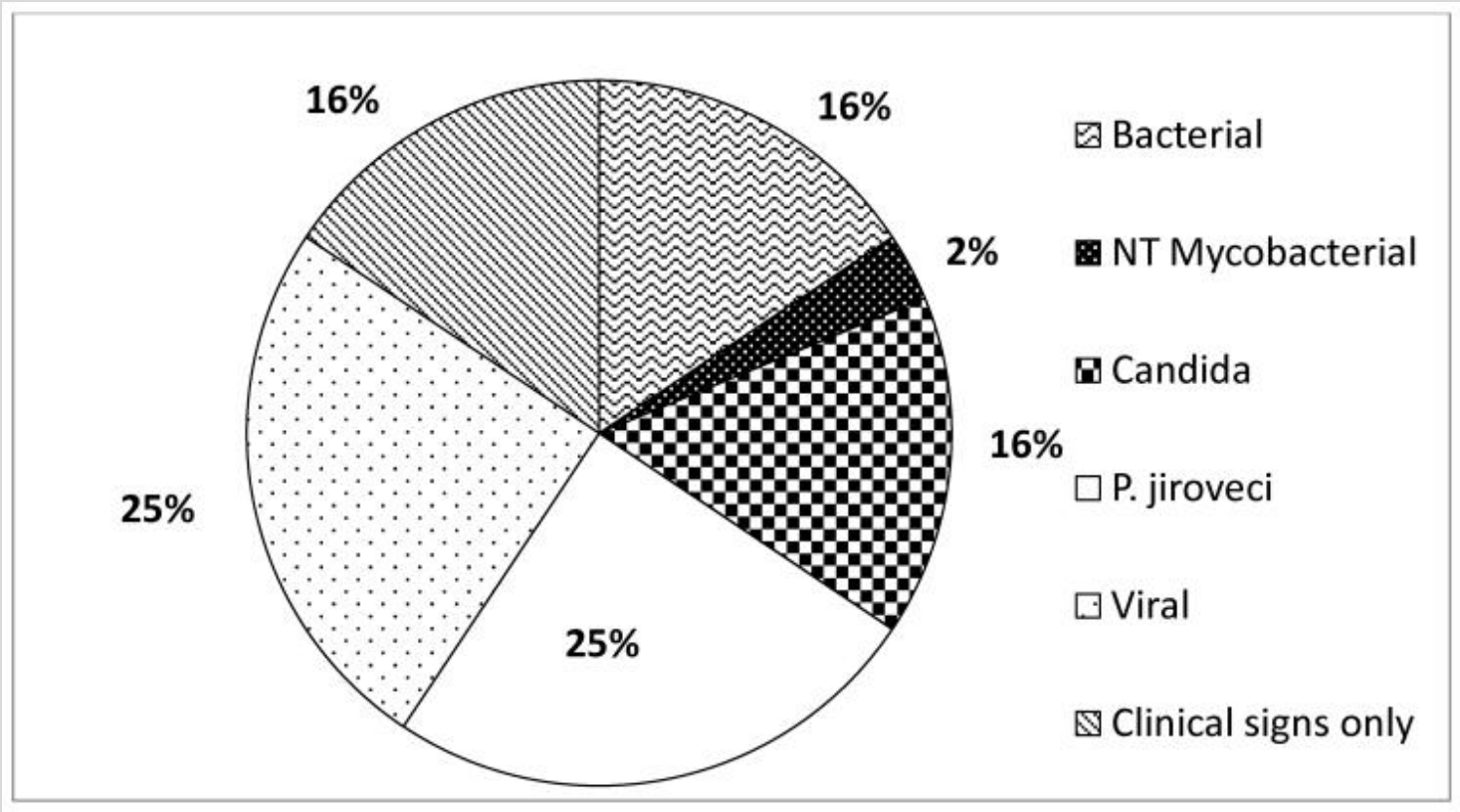
OS by Infection[2]

HSCT=hematopoietic cell transplant; MMRD=mismatched related donor; MSD=matched sibling donor; SCID=severe combined immunodeficiency; UCB=umbilical cord blood.

1. Pai SY, et al. *N Engl J Med*. 2014;371(5):434-446.
2. Heimall J, et al. *Blood*. 2017;130(25):2718-2727

Range of Opportunistic Pathogens in SCID

- Viral (25%) including respiratory syncytial virus, rotavirus and enterovirus, also P. jiroveci (25%)
- Bacterial infections (16%) including Pseudomonas, Streptococcus and Staphylococcus, and nontuberculous Mycobacteria (2%)
- Fungal (Candida - 16%)

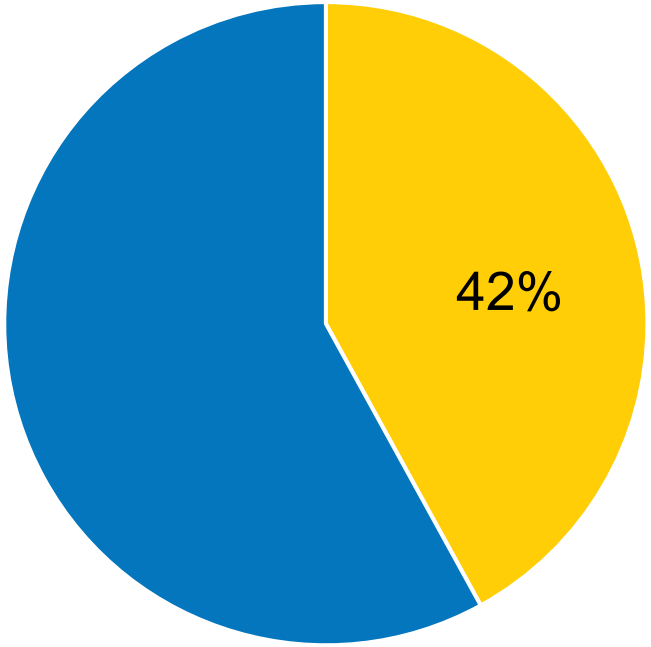


Source: Primary Immune Deficiency Treatment Consortium (N=50 patients with SCID)

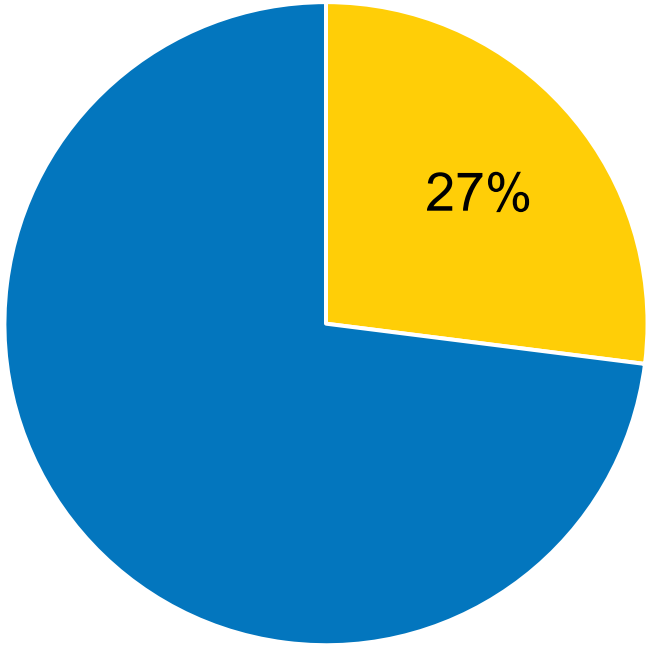
Dvorak CC, *J Clin Immunol*. 2013;33(7):1156-1164.

Patients are Susceptible to Risk of Infection Until HSCT

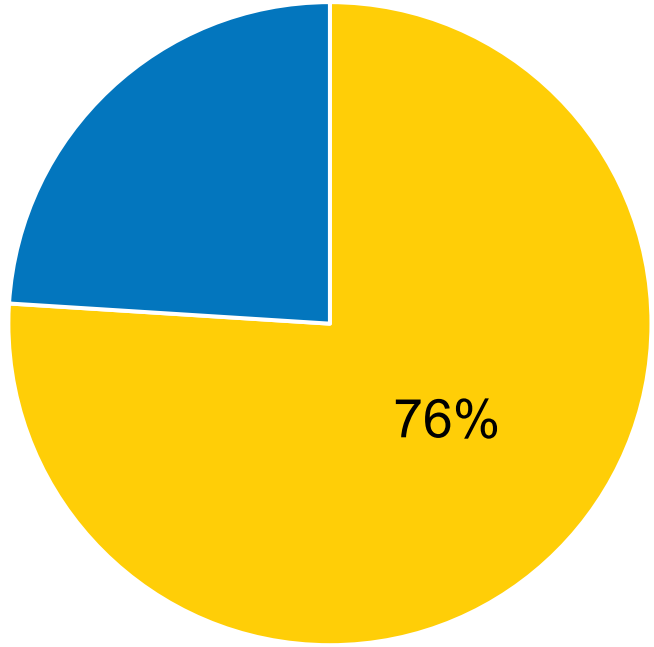
≥1 infection prior to HCT



Active infection at time of transplant



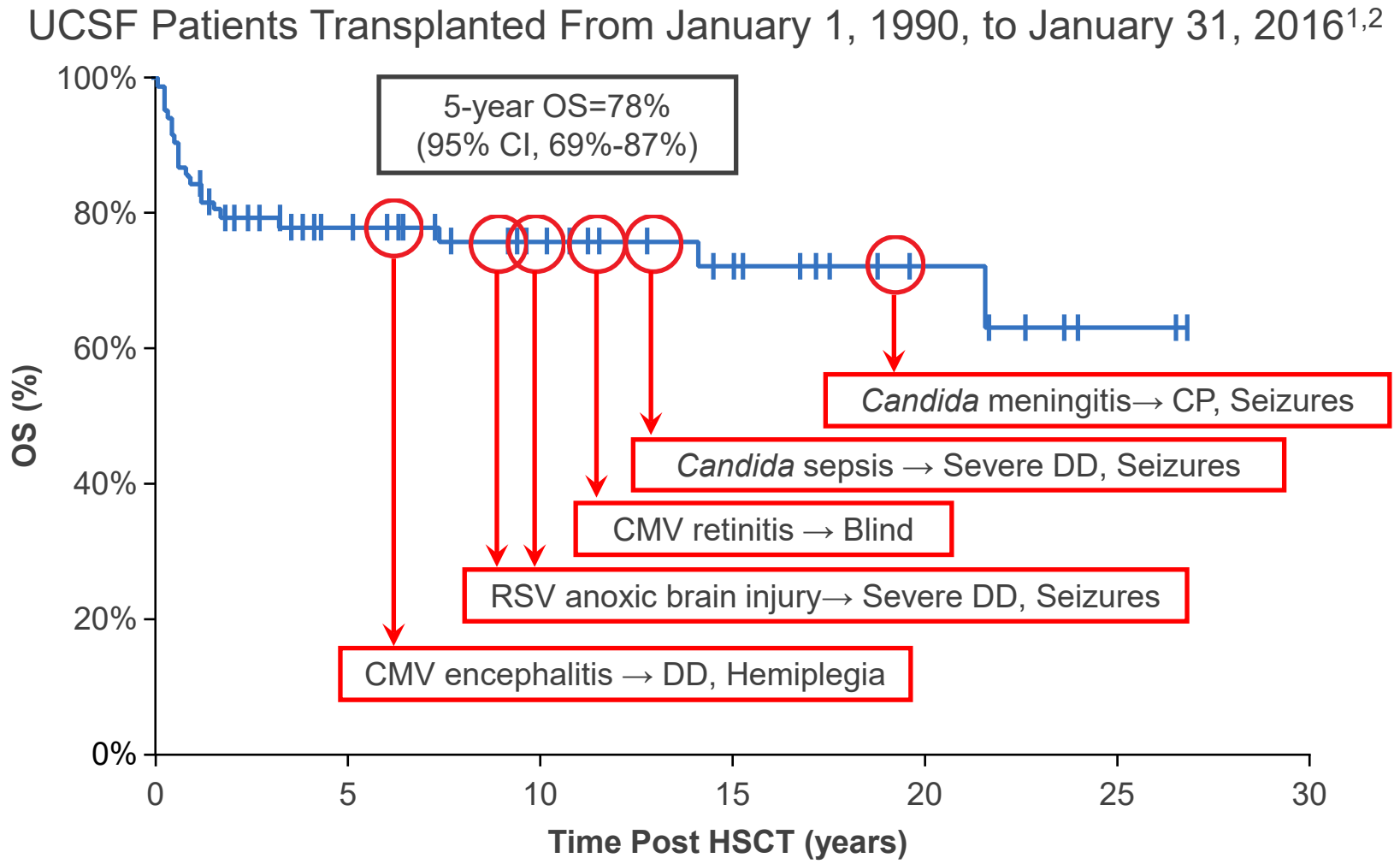
Infections developed between confirmatory testing and transplant



- Most common infections were: double-stranded DNA viral infections (n=10), respiratory viral infections (n=9), staphylococcus (n=7), *candida* (n=5), gram-neg rods (n=4), and C. difficile (n=4)
- Timing of HSCT from diagnosis was similar between those with infection vs those without, 77 and 66 days, respectively

HSCT=hematopoietic stem cell transplant; NBS=newborn screening.
Heimall J, et al. *Blood.* 2017;130(25):2718-2727.

Long Term Sequelae Secondary to Infections in SCID



CMV=cytomegalovirus; HSCT=hematopoietic stem cell transplant; OS=overall survival; RSV=respiratory syncytial virus; SCID=severe combined immunodeficiency; DD=Developmental Disability UCSF, University of California San Francisco.

1. Dvorak CC. Presented at Transplantation & Cellular Therapy Meetings; February 8-12, 2021.
2. Dvorak CC, et al. *Blood Adv*. 2017;1(20):1694-1698.

PIDTC Recommendations for Prophylaxis in SCID

Medication	Dose	Notes
Immunoglobulin replacement	400–600 mg/kg every 4 weeks for intravenous administration 100–150 mg/kg weekly for subcutaneous administration	Start within a few weeks of life. Maintain IgG trough > 800 mg/dL
PJP prophylaxis		
TMP/SMX	2.5 mg/kg TMP component PO BID twice weekly	Start when infant > 30 days old; monitor bilirubin and CBC
Pentamidine	4 mg/kg per dose IV every 2 weeks	If < 30 days old and high risk; give once, then re-evaluate in 2 weeks
Folinic acid	1.25 mg QD twice a week	Used to minimize TMP/SMX neutropenia
Valganciclovir for CMV prophylaxis	Valganciclovir 16 mg/kg PO QD	Start immediately only if there are clinical indications, such as abnormal physical exam or liver abnormalities. Otherwise, wait for mother's CMV IgG. If mother CMV IgG+, give valganciclovir until infant weekly blood PCR CMV is neg ×4 and then stop, provided infant remains well and CMV PCR negative May elect not to not treat if mother CMV negative and infant healthy
Acyclovir for HSV prophylaxis	Acyclovir 12.5 mg/kg PO BID or 8 mg/kg IV q12hr (≤ 12 kg)	Start immediately only if HSV risk identified; do not give in addition to valganciclovir
Fluconazole for fungal prophylaxis	3 or 6 mg/kg/day PO QD; check NICU dose for infants younger than 30 days	Start immediately; ensure normal LFTs prior to starting and follow
Palivizumab	Per institutional protocol, monthly	During RSV season

BID=twice a day; CMV=cytomegalovirus; IgG=immunoglobulin G; LFT=liver function test; NICU=neonatal intensive care unit; PCR=polymerase chain reaction; PIDTC=Primary Immune Deficiency Treatment Consortium; PJP=pneumocystis jirovecii pneumonia; PO=orally; QD=every day; RSV=respiratory syncytial virus; TMP-SMX=trimethoprim-sulfamethoxazole.

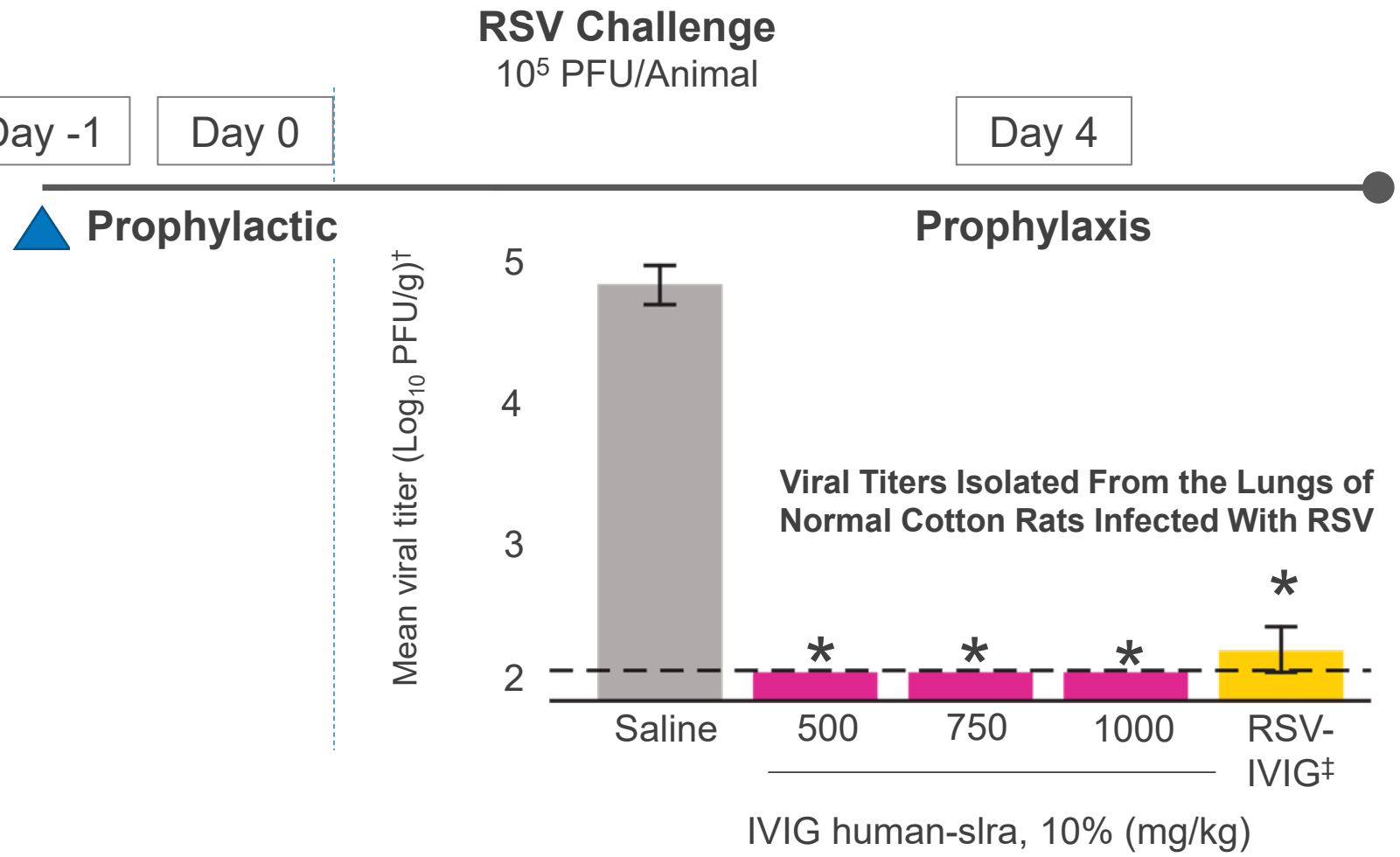
Dorsey MJ, et al. *J Clin Immunol*. 2021;41(1):38-50.

CLINICAL RATIONALE FOR IVIG IN SCID

Evaluation of IVIG human-slra, 10% in the Cotton Rat Model with RSV Infection

Viral lung titers in normal cotton rats*

Viral lung titers and histopathology from normal and immunosuppressed cotton rats



**P*<0.05 when compared with RSV-infected animals treated with saline.

*Immunosuppressed animals received repeated cyclophosphamide injections (IM or IP) at 50 mg/kg for 21 days prior to RSV infection and continuing throughout the post-infection period.
RSV=respiratory syncytial virus. ‡Historical IVIG product produced from hyperimmune donors.
Boukhvalova M, et al. *Bone Marrow Transplant*. 2016;51(1):119-126.

IVIG human-slra, 10% Composition and Characteristics[1,2]

PROPRIETARY TESTING

- A proprietary microneutralization assay is used to quantitatively measure neutralizing RSV antibodies in donor plasma

SCREEN AND IDENTIFY HIGH-TITER DONORS

- Identify donors with **high-titer antibodies to RSV**
- High-titer RSV donor also had increased titers to **8 other common respiratory viruses**

TAILORED COMPOSITION

- Uniquely blended plasma pools derived from ≥1000 donors that **meet FDA CFR Criteria** (a polyclonal IVIG with potency **for polio, measles, and diphtheria**) with a unique blend of normal source plasma plus RSV plasma
- Tailored pools exhibit **high titers of anti-RSV antibody**

CFR=Code of Federal Regulations; FDA=Food and Drug Administration; IVIG=intravenous immune globulin; RSV=respiratory syncytial virus.

1. Wasserman RL, et al. *Immunotherapy*. 2019;11(16):1423-1433. 2. Wasserman RL, et al. *Expert Rev Clin Immunol*. 2017;13(12):1107-1119.

Summary of Therapeutic Product Attributes*

	IVIG human-slra, 10% [1-3]	Standard IVIG[3,4]	Palivizumab[5,6]
Standardized antibody levels for RSV	✓	—	✓
High titers to other respiratory viruses	✓	—	—
Anti-inflammatory properties	✓	✓	—
Provide Ig replacement therapy	✓	✓	—
No demonstrated viral mutation and resistance	✓	✓	—
Meets FDA CFR criteria for potency for polio, measles, and diphtheria	✓	✓	—

IVIG=intravenous immune globulin; RSV=respiratory syncytial virus. *(Not a direct comparison)

1. ASCENIV Prescribing Information, ADMA Biologics, 2019. 2. Orange JS, et al. *Front Immunol*. 2015;6:431. 3. Durandy A, et al. *Clin Exp Immunol*. 2009;158(Suppl 1):2-13. 4. Kelesidis T, et al. *BMC Infect Dis*. 2014;14:321. 5. Papadopoulos NG, et al. *J Allergy Clin Immunol*. 2017;140(4):921-932. 6. Bates JT, et al. *Virology*. 2014;454-455:139-144. 7. Kennedy DA, Read AF. *Proc Natl Acad Sci U S A*. 2018;115(51):12878-12886.

COST ANALYSIS STUDY

Study Objective and Methodology

Objective

- To characterize the comparative costs of a unique IVIG human-slra 10% containing high titers of RSV-neutralizing antibodies and other respiratory pathogens to standard IVIG+palivizumab

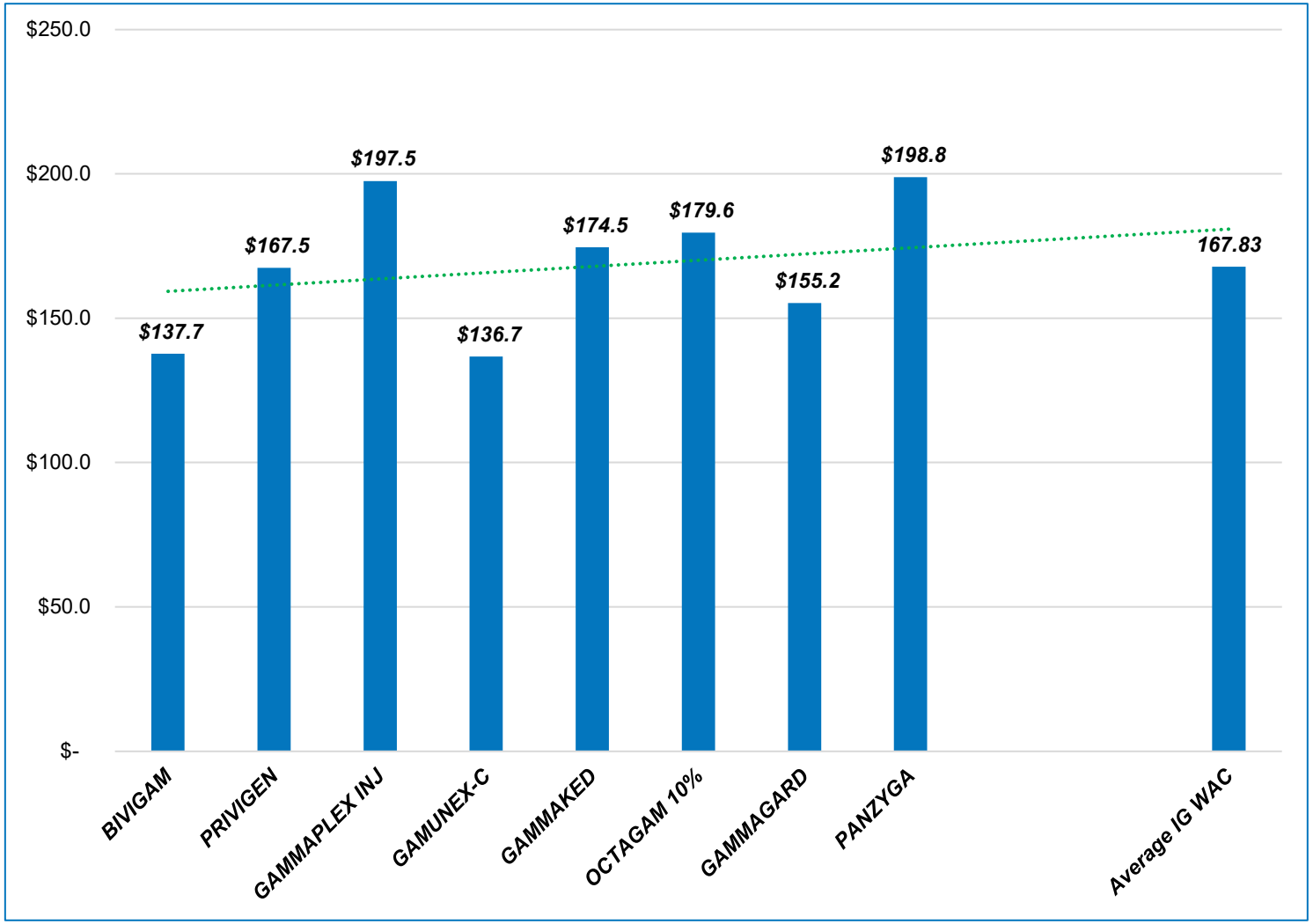
Methodology and Sample

- Pharmacoeconomic analysis across eight commercially available IVIG products at equivalent dosing and interval + palivizumab 15 mg/kg/month.
- 3-month-old SCID infant (6 kg) with history of infections awaiting transplant
- Cost basis determined using wholesale acquisition costs (WAC) sourced from Micromedex® RED BOOK
- WAC obtained for IVIG human-slra 500 mg/kg every 4 weeks compared to a composite average of WAC for commercial IVIG

Results: WAC pricing for standard 10% IVIG

WAC cost per gram for standard 10% IVIG varies across all manufacturers

- WAC cost/gram varies from $136.74/gram to $198.84/gram
- $167.83/gram mean cost of standard 10% IVIG across 8 different commercially available FDA products
- $927.18/gram WAC price for IVIG human-slra 10%

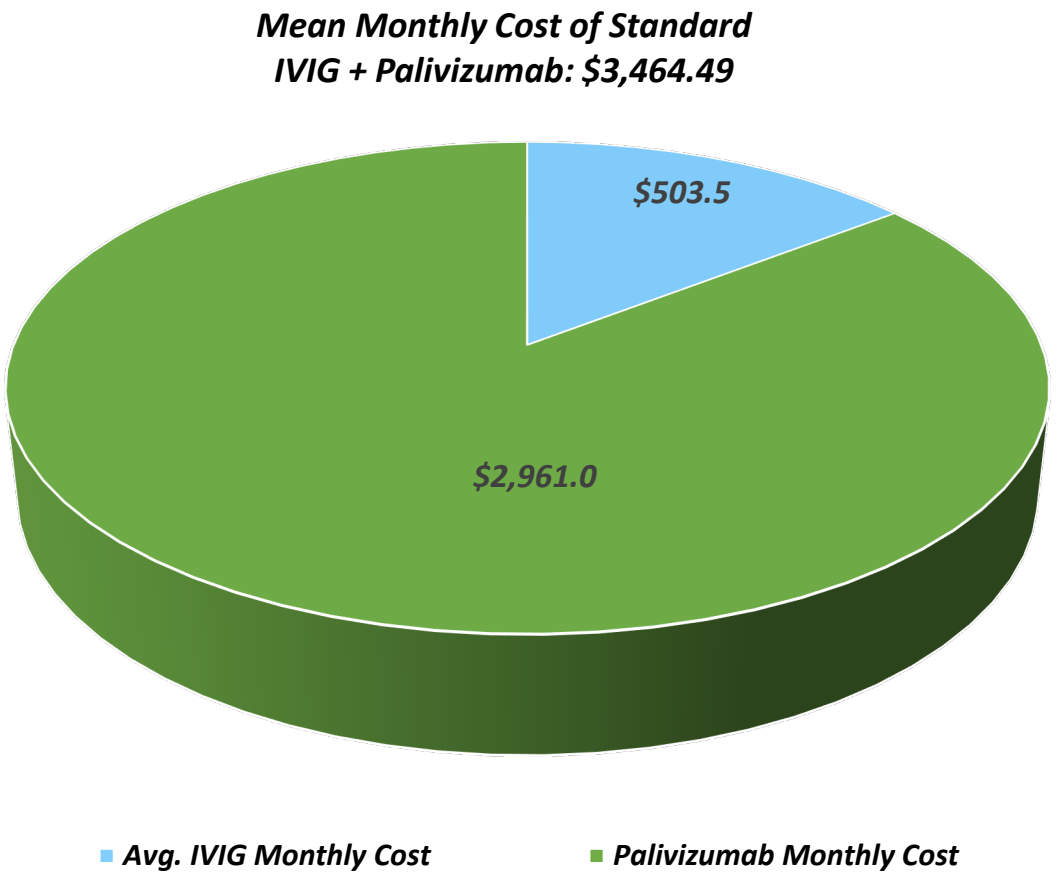


*All WAC pricing data from MICROMEDEX Red Book, dated January 9, 2023.

Results: WAC pricing for standard 10% IVIG + Palivizumab in Patient Model

Mean WAC cost for standard 10% IVIG across 8 different available brands is $167.83

- Monthly WAC of standard 10% IVIG for a 6-kg SCID baby is approximately $503.50 per month, using a mean WAC of $167.83/gram
- Palivizumab WAC is $32.90/mg
  - With recommended dosing of 15 mg/kg, 6-kg patient receives monthly dose of 0.90 mL (WAC $2,961.00/month)
- Total monthly WAC for standard 10% IVIG + Palivizumab therapy is $3,464.49
  - Represents >85% of the patient's monthly WAC cost of therapy



*All WAC pricing data from MICROMEDEX Red Book, dated January 9, 2023.

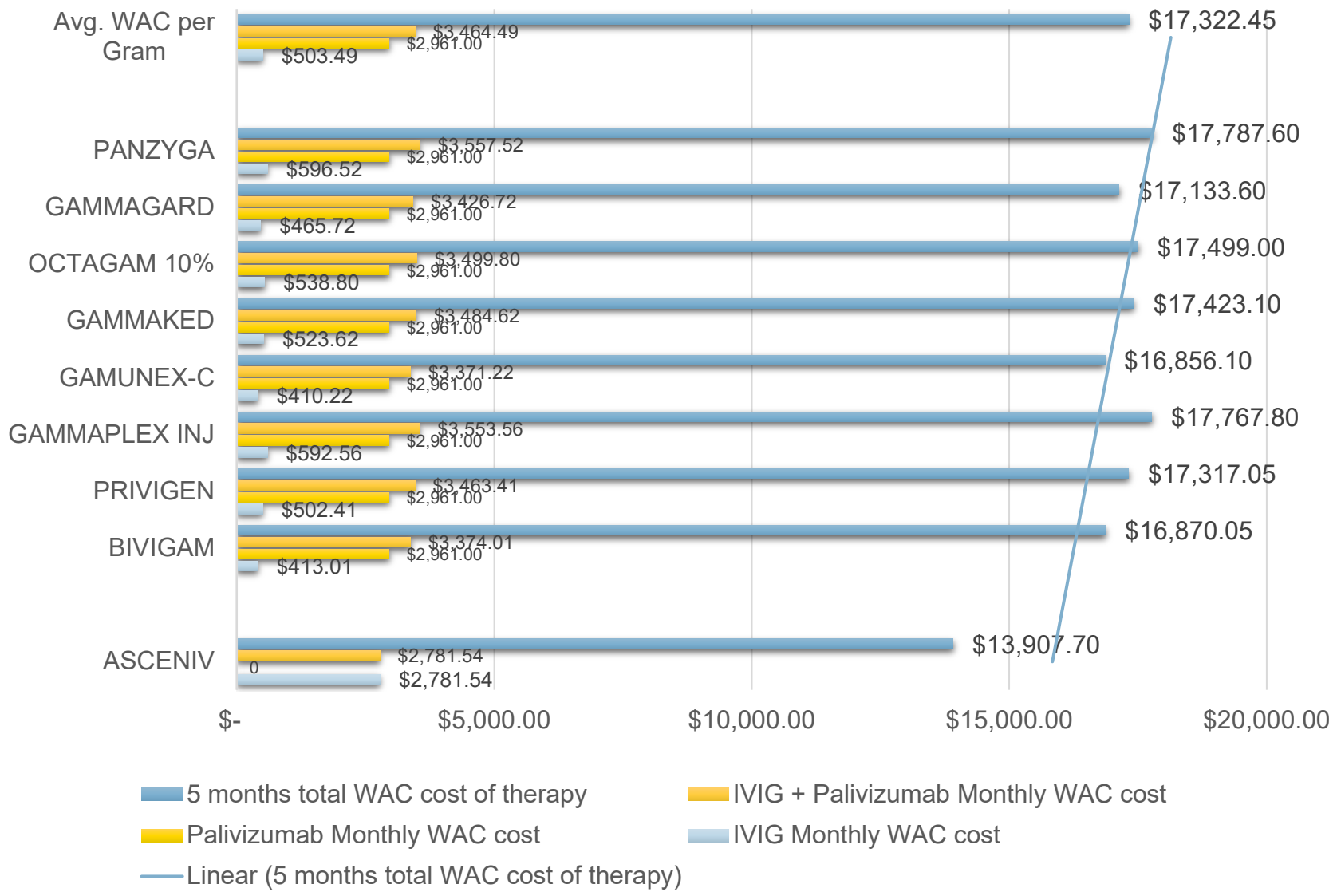
Results: Comparison of IVIG Human-slra 10% with Standard IVIG + Palivizumab in 6-kg SCID Infant

IVIG human-slra resulted in WAC of $13,907.70 vs $17,322.45 for standard IVIG+palivizumab, reflecting a 25% relative difference in cost of therapy

$17,322.45: WAC pricing for 5 months of standard 10% IVIG + Palivizumab

$13,907.70:5-months WAC pricing for IVIG human-slra 10

$3,414.75 in cost savings per SCID infant



*All WAC pricing data from MICROMEDEX Red Book, dated January 9, 2023.

Summary

- Despite current standard of care, SCID infants continue to experience serious infections, resulting in complications and poor outcomes
- Limited treatment modalities exist for the management of RVI in immunocompromised patients
  - An ideal therapeutic would enable restoration of the deficient humoral antibody compartment, as well as provide elevated antibodies to multiple respiratory pathogens
- Current cost analysis demonstrates favorable economic profile with IVIG human-slra,10%
  - Resulted in lower cost compared with the addition of palivizumab+standard IVIG
- Warrants further research to evaluate cost-effectiveness of IVIG human-slra,10% as a therapeutic alternative to IVIG + palivizumab

RVI=respiratory viral infection; SCID=severe combined immunodeficiency.

Thank you