

Preliminary Results of a Randomized Clinical Trial of Intravenous Immunoglobulin in Solid Organ Recipients with Severe Infection and Secondary Antibody Deficiency



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SPAIN

I **will** discuss off label use and investigational use of IVIG in SOT with HGG and severe infections

The following relevant financial relationships exist related to this presentation:

Presenting Author Javier Carbone: Grifols, USA, ISR Grant Principal Investigator.

Other authors: No relationships to disclosure



IgG Hypogammaglobulinemia is a risk factor of infection in SOT

SOT	Cut-Off HGG	Single Center	Sig Ass	Multi Center	Sig Ass	Rep	Author, study type (N), year
Heart	<600 <500 <400	4	4/4	1	1/1	+	Yamani ,SC (111) 2001; Yamani SC (300), 2005: Sarmiento SC (38), 2006; Sarmiento SC (75) 2009; Sarmiento MC (170), 2016
Lung	<700 <600 <400	5	4/5	1	1/1*	+	Goldfarb, SC (67) 2001; Kawut, SC (57) 2005; Yip, SC ,(40), 2006; Robertson, SC (32 Ped) 2009; Chambers, SC (139), 2013; Sarmiento, MC (82), 2017*
Kidney	<700 <650	4	3/4	1	1/1*	NT	Fernández-Ruiz, SC (226) 2012; Augusto, SC (318), 2016; Legris, SC (307) 2013; Pollock, SC (110) 1989; Sarmiento, MC (220), 2017*
Liver	<650 <700	3	2/3	ND	-	NT	Doron, SC, (112) 2006; Carbone, SC (34) 2009; Yoshizumi SC (177) 2014
SOT	<400	Metanalysis					Florescu, MET (1756) 2013

SOT solid organ transplantation. HGG: IgG hypogammaglobulinemia. NT Non tested. ND Not done. Sig Ass Significant association: Positive association/total of studies; Rep reproducibility of IgG testing in distinct centers; *Unpublished. Abstract available. SC Single center. MC Multicenter. MET Metanalysis.

Infection is a cause of death in solid organ transplantation. Secondary antibody deficiency is a risk factor of severe infection in solid organ transplantation. In a multicenter randomized clinical trial we evaluated the efficacy and safety of an intravenous immunoglobulin (IVIG) protocol to decrease the rate of re-infection in solid organ recipients with severe infections and secondary antibody deficiency.

- Adult patients (20 Heart, 12 Lung, 5 Kidney, 3 Liver Recipients) with post transplant severe infections and secondary antibody deficiency (IgG levels < 600 mg/dL at the time of the infectious complication) were included.
- IVIG protocol: Two doses of 15 grams followed by other 3 doses of 20 grams of a 5% IVIG product.
- 40 patients were randomized to receive IVIG in combination with conventional antimicrobial therapy (n=20) or conventional antimicrobial therapy alone (n=20).
- At the time of this preliminary report 36 patients that completed the protocol were analysed (17 IVIG + antimicrobial therapy, 19 antimicrobial therapy alone).
- Distinct specific antibodies were tested at the time of inclusion in the clinical trial and at the time of final visit (visit 7 at 30-45 days after last IVIG dose or similar time in no-IVIG patients) in a subgroup of patients to assess the kinetics of humoral immunity reconstitution.

RESULTS: Clinical Outcome and Immune Reconstitution

	IVIG	No IVIG	P
Clinical and Laboratory Parameters	N=17	N=19	
Primary outcome measure (rate of re-infection)	35.3	68.4	0.047
Time to reach normal IgG (IgG > 750 mg/dL)	55±44	93±42	0.06
Anticuerpos anti-CMV (Unidades)*	44398±12564	17519±9708	<0.001
Anti-toxina B de <i>clostridium difficile</i> (DO)*	0.26±0.08	0.09±0.03	<0.001
Anti-toxina A de <i>clostridium difficile</i> (DO)*	0.19±0.05	0.11±0.03	<0.001

* Immune reconstitution was evaluated at the Gregorio Marañón Hospital in Madrid

Increase of specific antibody titers in IVIG treated patients

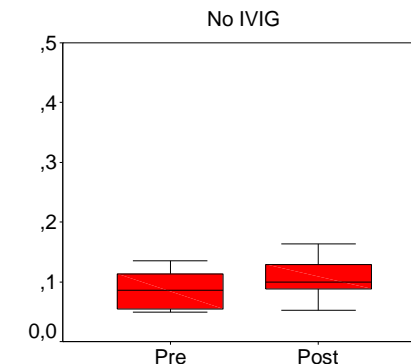
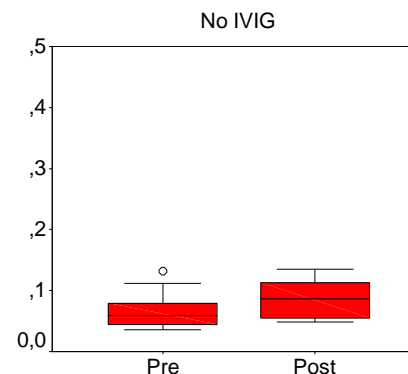
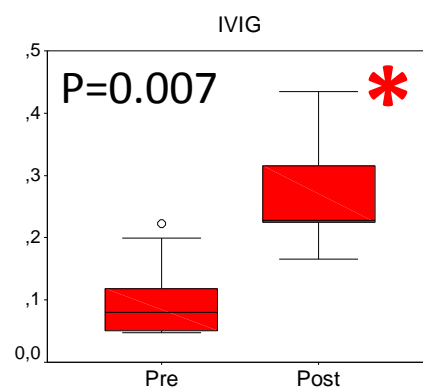
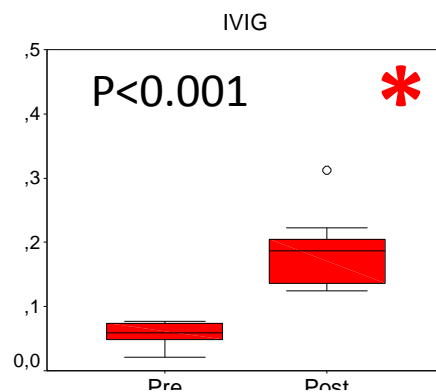
Pre= Visit 1

Post= Last Visit

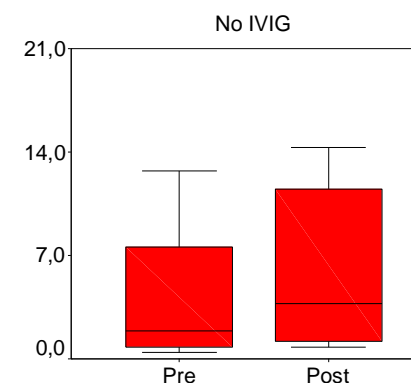
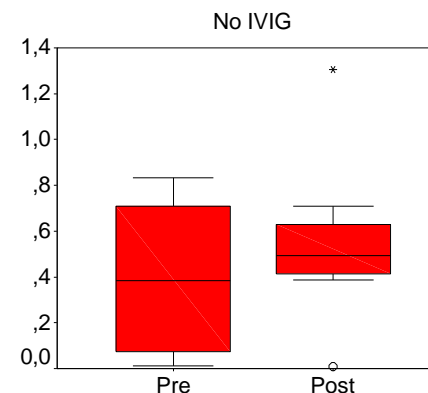
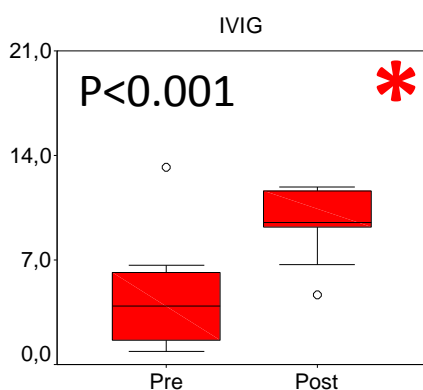
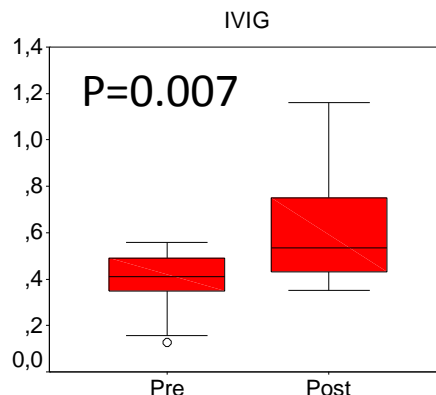
IVIG + antimicrobial therapy

Antimicrobial therapy alone

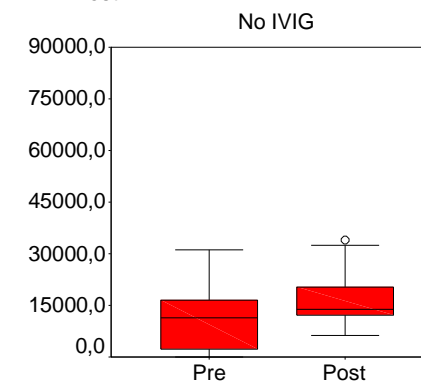
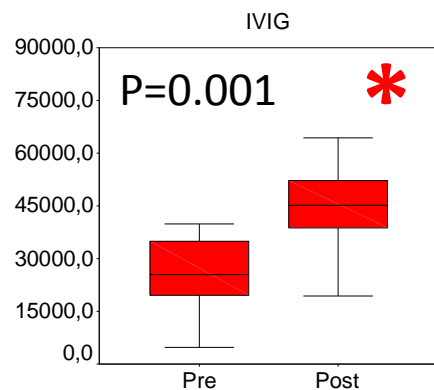
Anti-Clostridium
Difficile



Anti-Clostridium
Tetani IgG, IgG1



Anti-CMV



Conclusion

In a randomized clinical trial we have preliminarily demonstrated that IVIG is associated with reconstitution of distinct specific antibodies and with a lower rate of re-infection in solid organ transplantation with severe infection and secondary antibody deficiency.