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Analytical robustness and clinical consistency evaluation of a new IVD biotechnological immunoassay to help decision-making in adjustment of immunosuppressant therapy for kidney transplantation: TRANSBIO STUDY

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Introduction

Kidney transplanted (KT) patients have a persistent risk of graft rejection and require long term treatment with immunosuppressive drugs (IMS). IMS can also lead to severe side effects. There is a clinical need for tools to support clinicians when adjusting IMS treatment in each patient.
Immunobiogram (IMBG) is a blood-based in vitro pharmacodynamic test developed *by Biohope* that offers a personalized comparative evaluation of patient´s level of sensitivity/resistance to most used IMS

Objectives

TRANSBIO study is an observational, international and multicentre clinical study that aims to evaluate IMBG robustness to measure patient sensitivity/resistance pattern to IMS in KT. IMBG intrasubject, inter-time consistency and association with patients´ clinical prognoses was measured.

Methods

IMBG is a 3D-cell culture of PBMCs in semi-solid matrix submitted to immune stimulation and exposed to an IMS concentration gradient along a channel. The capacity of IMS gradient to inhibit the activation cells state can be transformed into a dose/response curve for each IMS. Segmentation analysis based on Key Curve Parameters -Area Over the Curve (AOC) and Response at maximal IMS concentration (I∞)- allow for patient classification in IMBG sensitivity /resistance levels for each IMS. A semiautomatic model for IMBG data interpretation provides a **Global IMBG Score** and an **Expert IMBG Score** with the patients´sensitivity level to all IMS tested or only to the current IMS treatment respectively.

TRANSBIO study had 2 arms:
Arm 1: patients were allocated to a **Bad-Clinical-Evolution** group (**BCE**) if they had a progressive deterioration in renal function in last 18 months and objective signs of immunological rejection in biopsy and/ or dnDSA strength or to a **Good-Clinical-Evolution** (**GCE**), if they had no previous rejection episodes, no dnDSA, and a stable renal function and IMS treatment for the last 12 months.
Arm 2: set of clinically stable patients to test intra-subject and inter-time IMBG consistency by comparing three IMBG at baseline and after 1 month of follow up.

Results

Dataset of evaluable patients was n=103 for Arm 1 and n=61 for Arm 2.

- **Arm 1:** In the logistic regression analyses the IMBG level of resistance to the IMS that patients were taking measured with the **Expert IMBG Score (S++, S+, S, Normal, R, R+, R++)** was significantly associated with the probability to have a Bad Prognosis (**BCE)**
  OR:1.279 95%CI:1.038-1.577, p=0.021

- **Arm 2**: IMBG showed intrasubject and intertime consistency in terms of similarity with less than 20% and 30% variation in the AOC value (Table 1&2). For ID50 the % of variation were slightly higher than these.

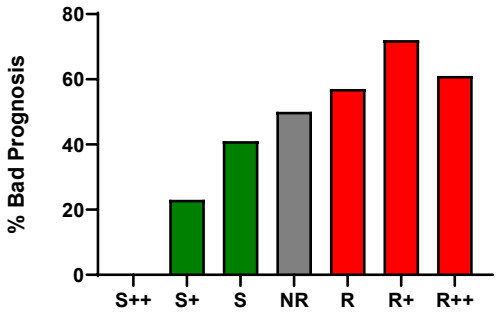

Table 1. Intra-subject consistency AOC

	N	Mean (all subjects & visits)	Lower LA	Upper LA	1.96*within subject SD/ Mean(all)
MMF	93	71.94	65.10	78.79	9.51%
CSA	93	76.39	68.92	83.87	9.79%
TAC	96	67.29	59.29	75.29	11.89%
PRD	96	64.63	55.60	73.67	13.98%
SIR	94	68.99	61.03	76.95	11.54%
EVE	95	64.80	57.68	71.92	10.99%
AZA	96	73.32	63.47	83.17	13.43%

Table 2. Inter-subject consistency AOC

	N	Mean (V1-V2)	Lower LA	Upper LA	1.96*SD (V1-V2)/ Mean(all)
MMF	34	-0.67	-15.08	13.73	20.04%
CSA	36	0.31	-11.64	12.27	15.62%
TAC	37	0.54	-13.73	14.82	21.32%
PRD	36	-0.77	-18.78	17.25	27.79%
SIR	36	0.21	-11.69	12.10	17.23%
EVE	37	-0.18	-10.98	10.62	16.64%
AZA	38	-0.38	-17.04	16.28	22.72%

LA: limits of agreement. Subjects with ≥ 2 fitted IMBG curves, different times treated as different subjects

Conclusions

IMBG allows to quantify in vitro patients´ PBMC sensitivity/resistance profile to a panel of IMS in Kidney Transplantation recipients. TRANSBIO study will provide conclusive results about robustness, reliability and clinical performance of IMBG.