

# Complement Activating anti-HLA DSA and Solid Organ Transplant Survival

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www.paristransplantgroup.org



Paris Translational Research Center for Organ Transplantation



## THE PREVALENT ORGAN TRANSPLANT UNIVERSE

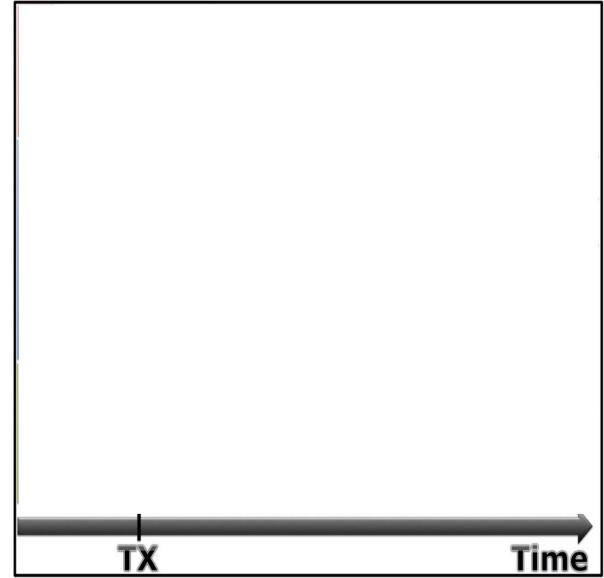
# 1,000,000

(700,000 kidneys) 80,000 <u>new</u> kidney transplants per year

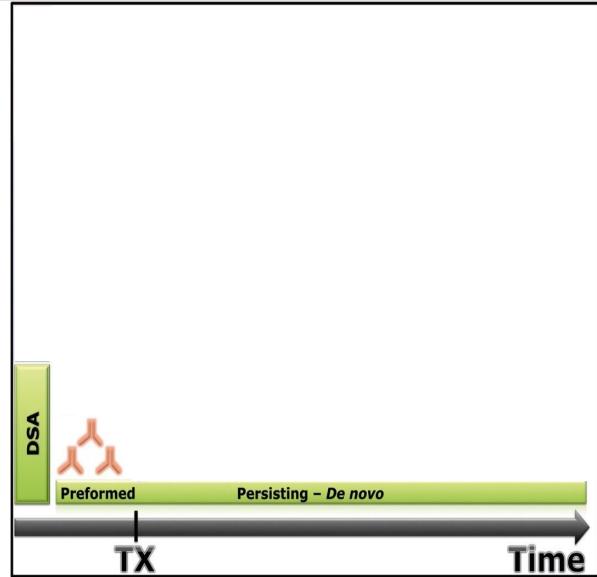
# About 15% have DSA: 150,000 About half have ABMR: 75,000



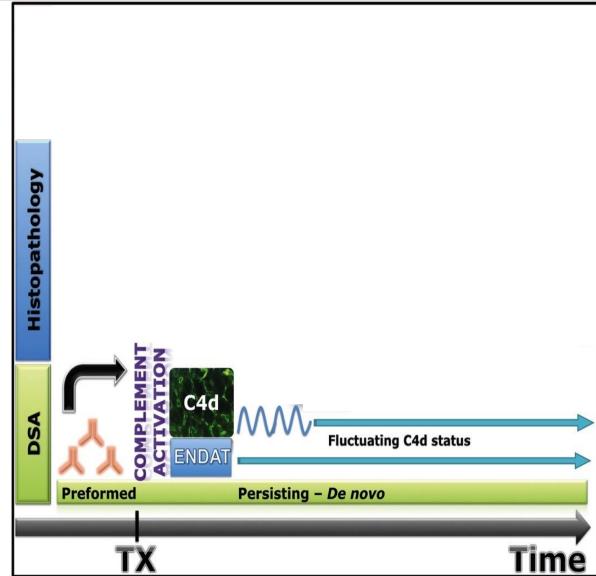
#### **INJURY**



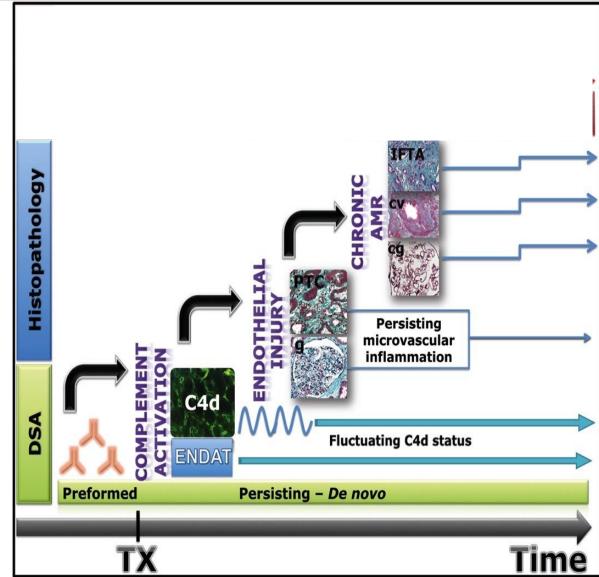
#### **INJURY**



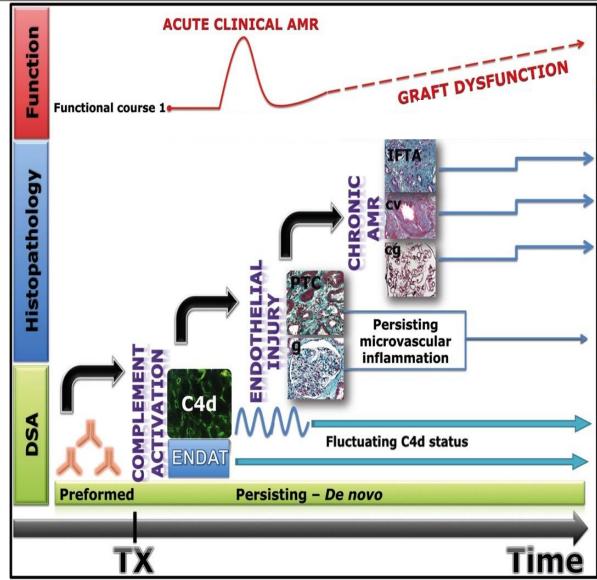
#### **INJURY**



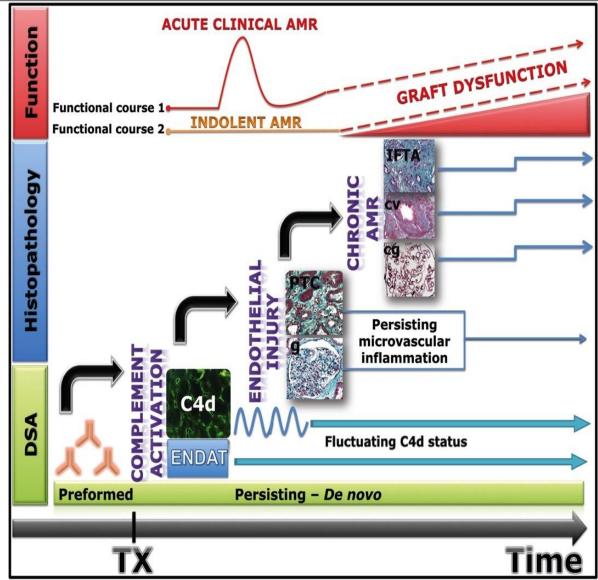
#### **INJURY**



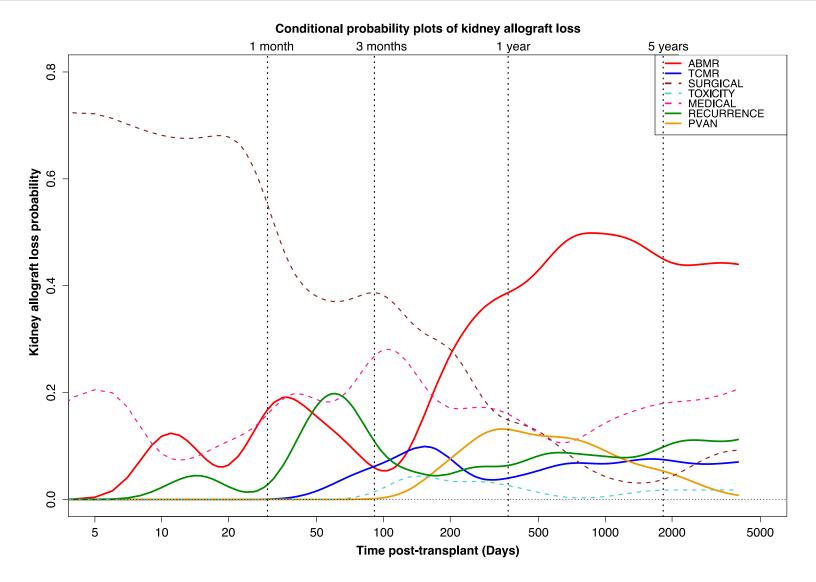
**INJURY** 



**INJURY** 



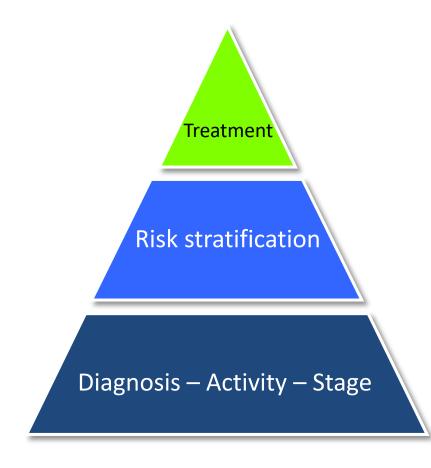
#### ABMR IS THE MAIN CAUSE OF LATE ALLOGRAFT LOSS





Loheac C & Aubert O et al. Unpublished data

## WHAT NEED TO BE ACHIEVED

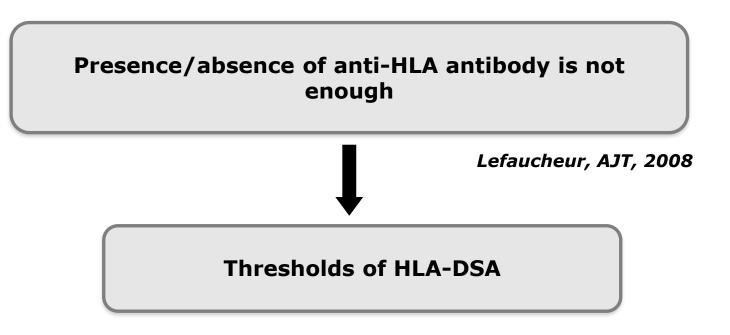


#### Washington, Sept 28<sup>th</sup> 2015



- ABMR = current outstanding matter of concern
- ✓ Reponse to therapy in ABMR is unknown
- ✓ PHENOTYPES ARE MANDATORY
- $\checkmark$  Precision composite end point is needed

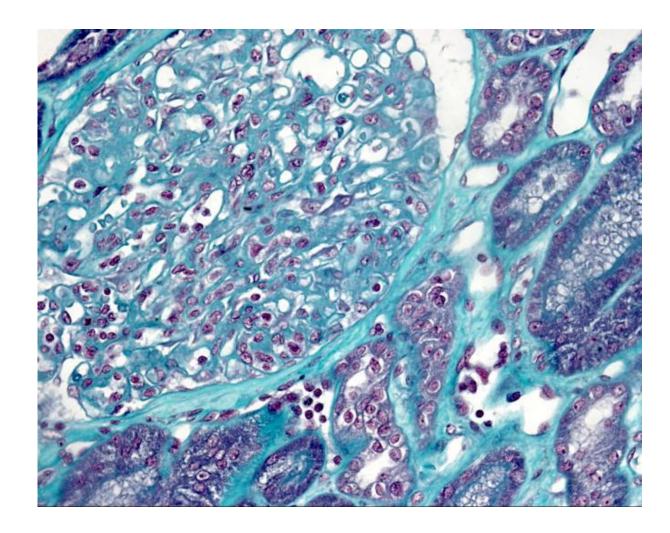




Lefaucheur & Loupy, JASN, 2010



### ARE DSA EQUAL?



## Miss C. 3<sup>rd</sup> graft

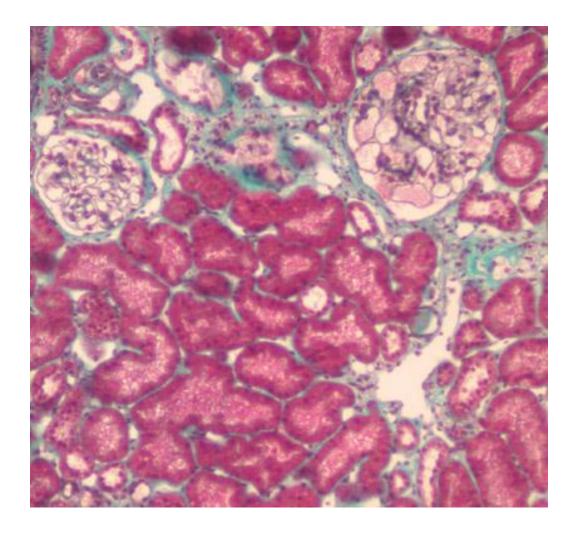
# DSA DQ2 MFI 2460



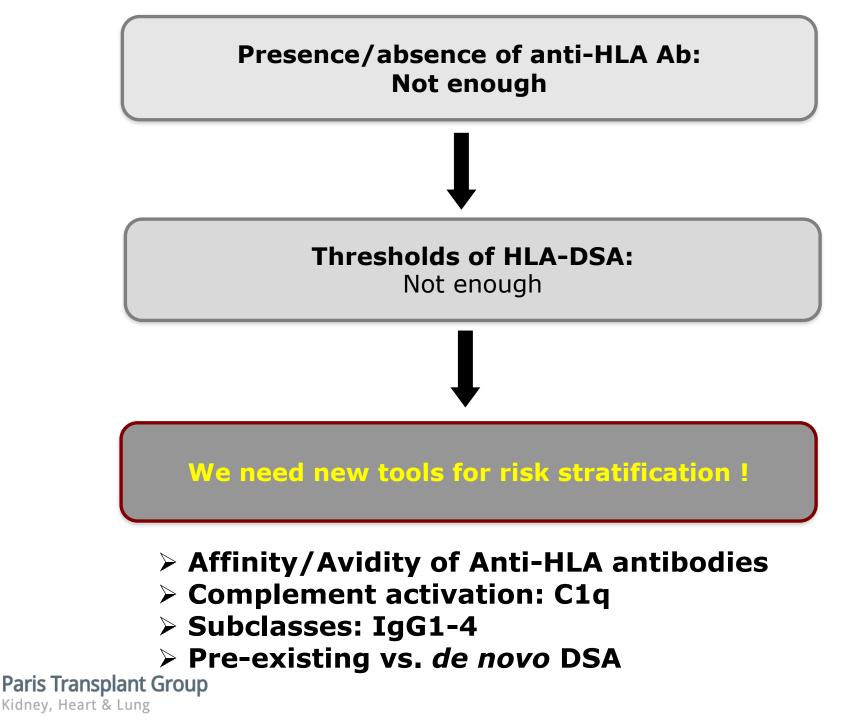
### ARE DSA EQUAL?

# Mr D 1<sup>st</sup> graft

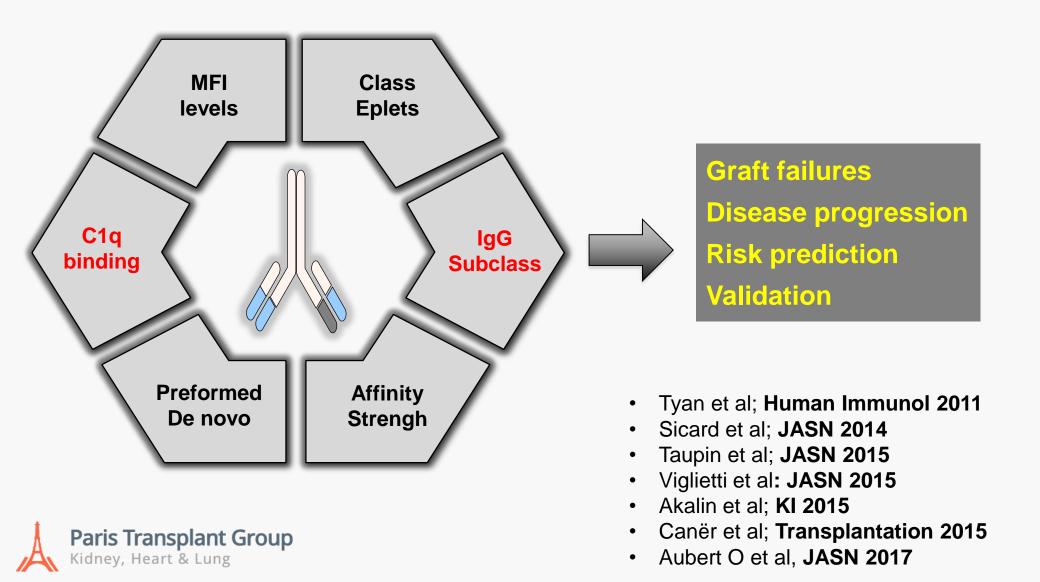
# DSA DR 7 MFI 3800







# Integrative and multiplex assessment of DSA



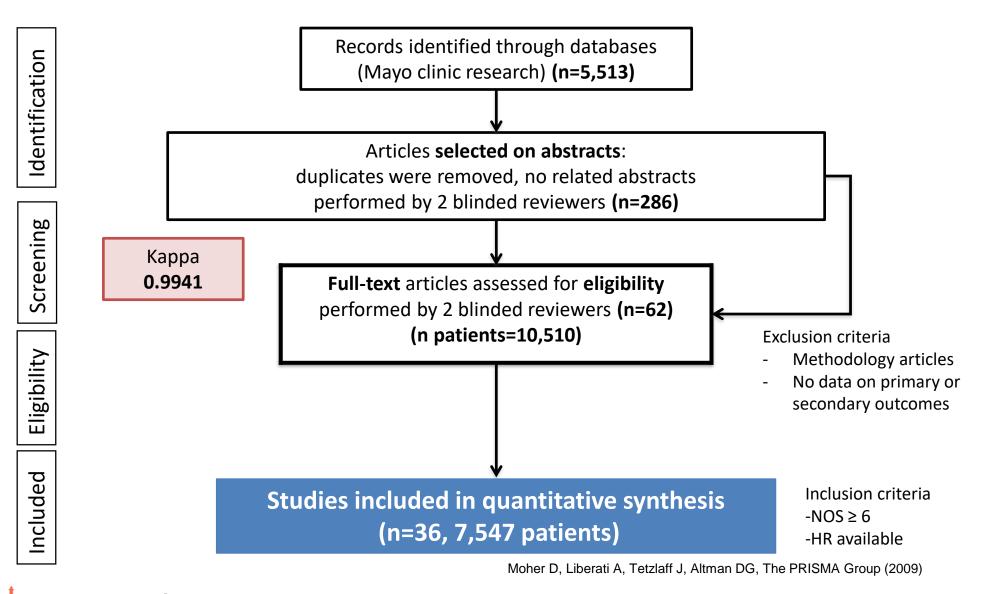
# Anti-HLA DSA characteristics associated with risk of allograft loss

### Complement binding capacity

IgG subclass composition



# Meta-Analysis: Clinical Significance of Complement Activating Anti-HLA DSA in Kidney Transplantation





#### Loheac C, Aubert O et al PLOS MEDICINE IN PRESS

# Meta-Analysis: Clinical Significance of Complement Activating Anti-HLA DSA in Kidney Transplantation

Studies P	Overall Population	Patients Without DSA	Patients with Non complement activating DSA	Patients with complement activating DSA	HR (95% CI) % We	eight
Wahrmann et al. (2009)	338	299	18	21	2.40 (0.90, 6.00) 3.1	15
Sutherland et al. (2011)	35	0	20	15	5.80 (1.40, 22.90) 1.7	71
Smith et al. (2011)	243	195	22	26	3.02 (1.11, 8.23) 2.9	91
Kaneku et al. (2012)	39	0	24	12	3.35 (1.39, 8.05) 3.5	51
Crespo et al. (2013)	355	327	13	15	0.83 (0.17, 4.14) 1.3	35
Freitas et al. (2013)	203	149	30	24	3.50 (1.30, 9.50) 2.9	94
Loupy et al. (2013)	1016	700	23 <mark>9</mark>	77	4.78 (2.69, 8.49) 5.7	77
Smith et al. (2014)	63	36	18	9	6.43 (2.96, 13.97) 4.1	13
Everly et al. (2014)	179	132	22	25	2.48 (1.02, 6.04) 3.4	45
Arnold et al. (2014)	274	180	20	74	4.81 (1.65, 14.03) 2.6	63
O'Leary et al. (2015)	1270	1086	13 <mark>1</mark>	53	2.40 (1.82, 5.75) 5.7	77
Sicard et al. (2015)	69	0	29	40	2.80 (1.12, 6.95) 3.3	33
Khovanova et al. (2015)	80	0	45	35	1.69 (0.41, 6.93) 1.6	69
O'Leary et al. (2015)	1270	1086	90	94	1.90 (1.62, 3.45) 7.9	95
Khovanova et al. (2015)	80	0	53	27	2.09 (0.30, 14.60) 0.9	95
Sicard et al. (2015)	69	0	35	30	1.98 (0.95, 4.14) 4.4	41
Bamoulid et al. (2016)	59	0	23	36	6.78 (0.86, 53.50) 0.8	86
Visentin et al. (2016)	53	25	16	12	<b>1.65 (0.68, 3.97)</b>	49
Kauke et al. (2016)	611	571	13	27	3.77 (1.40, 10.16) 2.9	96
Calp-Inal et al. (2016)	284	253	20	11	4.30 (1.10, 16.50) 1.8	81
Comoli et al. (2016)	114	0	105	9	● 27.80 (5.61, 137.72) 1.3	36
Fichtner et al. (2016)	62	36	17	9	6.35 (1.33, 30.40) 1.4	41
Lefaucheur et al. (2016)	125	0	90	35	4.80 (1.70, 13.30) 2.8	80
Lefaucheur et al. (2016)	125	0	73	52	3.60 (1.10, 11.70) 2.2	26
Comoli et al. (2016)	114	0	89	25	11.09 (2.25, 54.64) 1.3	36
Guidicelli et al. (2016)	346	321	13	12	2.99 (0.94, 10.27) 2.2	22
Sicard et al. (2017)	52	0	31	21	3.71 (1.27, 10.80) 2.6	63
Couchonnal et al (2017)	100	76	6	18	4.12 (0.95, 17.89) 1.5	58
Viglietti et al. (2017)	851	665	129	57	3.60 (1.71, 7.59) 4.3	
Moktefi et al. (2017)	48	0	25	20	0.79 (0.25, 2.44) 2.3	39
Bibhuti et al. (2017)	127	68	22	37	3.20 (1.34, 7.86) 3.4	48
Wiebe et al. (2017)	70	0	53	17		
Viglietti et al. (2017)	851	665	144	42	4.25 (1.88, 9.61) 3.8	
Bailly et al. (2017)	25	0	8	17	3.70 (0.80, 17.00) 1.4	
Overall (I-squared = 29.8	5%, p = 0.05	56)				0.00
NOTE: Weights are from	random effe	ects analysi	s			

Kidney, Heart & Lung

#### C' activating Ab: multiorgan relevance





Studies	Overall Population	Patients Without DSA	Patients with Non complement activating DSA	Patients with complement activating DSA		HR (95% Cl) % Weig
Heart, lung and l	liver					
Smith et al. (2011)	243	195	22	26		3.02 (1.11, 8.23) 2.9 <sup>-</sup>
Kaneku et al. (2012	2) 39	0	24	12		3.35 (1.39, 8.05) 3.5
Smith et al. (2014)	63	36	18	9	•	6.43 (2.96, 13.97) 4.13
D'Leary et al. (2015	5) 1270	1086	131	53		2.40 (1.82, 5.75) 5.73
D'Leary et al. (2015	,	1086	90	94		1.90 (1.62, 3.45) 7.9
/isentin et al. (2016	,	25	16	12		1.65 (0.68, 3.97) 3.49
Couchonnal et al (2		76	6	18	-	4.12 (0.95, 17.89) 1.58
Bibhuti et al. (2017)		68	22	37		3.20 (1.34, 7.86) 3.48
Subtotal (I-squared					$\diamond$	2.71 (1.98, 3.72) 32.8
Kidney						
vahrmann et al. (20	009) 338	299	18	21	<b>↓</b>	2.40 (0.90, 6.00) 3.15
Sutherland et al. (20	011) 35	0	20	15		5.80 (1.40, 22.90) 1.7
respo et al. (2013	) 355	327	13	15		0.83 (0.17, 4.14) 1.3
reitas et al. (2013)	) 203	149	30	24		3.50 (1.30, 9.50) 2.9
oupy et al. (2013)	1016	700	239	77		4.78 (2.69, 8.49) 5.7
verly et al. (2014)	179	132	22	25	••••	2.48 (1.02, 6.04) 3.4
mold et al. (2014)	274	180	20	74		4.81 (1.65, 14.03) 2.6
icard et al. (2015)		0	29	40		2.80 (1.12, 6.95) 3.3
hovanova et al. (2		0	45	35	•	1.69 (0.41, 6.93) 1.6
hovanova et al. (2		0	53	27	•	2.09 (0.30, 14.60) 0.9
Sicard et al. (2015)	69	0	35	30		1.98 (0.95, 4.14) 4.4
3amoulid et al. (20 <sup>-</sup>	16) 59	0	23	36	-	6.78 (0.86, 53.50) 0.8
(auke et al. (2016)	,	571	13	27		3.77 (1.40, 10.16) 2.9
Calp-Inal et al. (201		253	20	11		4.30 (1.10, 16.50) 1.8
omoli et al. (2016)	•	0	105	9	· · · · · · · · · · · · · · · · · · ·	27.80 (5.61, 137.72)1.3
ichtner et al. (2016	,	36	17	9		6.35 (1.33, 30.40) 1.4
efaucheur et al. (2	,	0	90	35		4.80 (1.70, 13.30) 2.80
efaucheur et al. (2	,	0	73	52		3.60 (1.10, 11.70) 2.20
Comoli et al. (2016)	,	0	89	25		11.09 (2.25, 54.64) 1.30
Guidicelli et al. (201		321	13	12	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	2.99 (0.94, 10.27) 2.23
Sicard et al. (2017)	,	0	31	21		3.71 (1.27, 10.80) 2.6
/iglietti et al. (2017		665	129	57		3.60 (1.71, 7.59) 4.3
Noktefi et al. (2017	,	0	25	20		0.79 (0.25, 2.44) 2.3
Viebe et al. (2017)	,	0	53	17		1.06 (0.50, 2.40) 4.00
iglietti et al. (2017)		665	144	42		4.25 (1.88, 9.61) 3.8
Bailly et al. (2017)	25	005	8	17		3.70 (0.80, 17.00) 1.4
Subtotal (I-squared		-	Ū	17	$\diamond$	3.20 (2.49, 4.11) 67.
Overall (I-squared	= 29.5%, p =	0.056)				3.05 (2.50, 3.72) 100
NOTE: Weights are	e from random	n effects an	nalysis			

#### C' activating Ab: Timing of Ab detection







Studies	Overall Population	Patients Without DSA	Patients with Non complement activating DSA	Patients with complement activating DSA	HR (95% Cl) % W
Pre-existing DSA					
Wahrmann et al. (2009	9) 338	299	18	21	2.40 (0.90, 6.00)
Crespo et al. (2013)	355	327	13	15	0.83 (0.17, 4.14)
Smith et al. (2014)	63	36	18	9	6.43 (2.96, 13.97)
O'Leary et al. (2015)	1270	1086	131	53	2.40 (1.82, 5.75)
Khovanova et al. (201	5) 80	0	45	35	1.69 (0.41, 6.93)
O'Leary et al. (2015)	1270	1086	90	94	1.90 (1.62, 3.45)
Subtotal (I-squared =	47.2%, p =	0.092)			2.42 (1.56, 3.76)
Pre-existing and c	le novo D	SA			
Kaneku et al. (2012)	39	0	24	12	3.35 (1.39, 8.05)
Loupy et al. (2013)	1016	700	239	77	4.78 (2.69, 8.49)
Sicard et al. (2015)	69	0	29	40	2.80 (1.12, 6.95)
Khovanova et al. (201	5) 80	0	53	27	2.09 (0.30, 14.60)
Sicard et al. (2015)	69	0	35	30	1.98 (0.95, 4.14)
Visentin et al. (2016)	53	25	16	12	1.65 (0.68, 3.97)
Fichtner et al. (2016)	62	36	17	9	6.35 (1.33, 30.40)
Lefaucheur et al. (201	6) 125	0	90	35	4.80 (1.70, 13.30)
_efaucheur et al. (201	,	0	73	52	3.60 (1.10, 11.70)
Sicard et al. (2017)	52	0	31	21	3.71 (1.27, 10.80)
Couchonnal et al (201	17) 100	76	6	18	4.12 (0.95, 17.89)
√iglietti et al. (2017)	851	665	129	57	3.60 (1.71, 7.59)
Voktefi et al. (2017)	48	0	25	20	0.79 (0.25, 2.44)
Viglietti et al. (2017)	851	665	144	42	4.25 (1.88, 9.61)
Bailly et al. (2017)	25	0	8	17	3.70 (0.80, 17.00)
Subtotal (I-squared =	0.0%, p = 0	.458)			3.18 (2.49, 4.05)
De novo DSA					
Sutherland et al. (2011	) 35	0	20	15	5.80 (1.40, 22.90)
Smith et al. (2011)	243	195	22	26	3.02 (1.11, 8.23)
Freitas et al. (2013)	203	149	30	24	3.50 (1.30, 9.50)
Everly et al. (2014)	179	132	22	25	2.48 (1.02, 6.04)
Arnold et al. (2014)	274	180	20	74	4.81 (1.65, 14.03)
Bamoulid et al. (2016)	59	0	23	36	6.78 (0.86, 53.50)
Kauke et al. (2016)	611	571	13	27	3.77 (1.40, 10.16)
Calp-Inal et al. (2016)	284	253	20	11	4.30 (1.10, 16.50)
Comoli et al. (2016)	114	0	105	9	27.80 (5.61, 137.72)
Comoli et al. (2016)	114	0	89	25	11.09 (2.25, 54.64)
Guidicelli et al. (2016)	346	321	13	12	2.99 (0.94, 10.27)
Bibhuti et al. (2017)	127	68	22	37	3.20 (1.34, 7.86)
Wiebe et al. (2017)	70	0	53	17	1.06 (0.50, 2.40)
Subtotal (I-squared =	38.0%, p =	0.081)			3.65 (2.45, 5.44)
Overall (I-squared = 2	29.5%, p = 0	.056)			3.05 (2.50, 3.72)
NOTE: Weights are fro	om random	effects ana	ysis		

#### C' activating Ab: type of test

Wahrmann et al. (2009) 338

Sutherland et al. (2011) 35

Bamoulid et al. (2016) 59

Lefaucheur et al. (2016)125

Guidicelli et al. (2016) 346

Smith et al. (2011)

Smith et al. (2014)

Crespo et al. (2013)

O'Leary et al. (2015)

Visentin et al. (2016)

Calp-Inal et al. (2016)

Fichtner et al. (2016)

Comoli et al. (2016)

Viglietti et al. (2017)

Moktefi et al. (2017)

Bibhuti et al. (2017)

Wiebe et al. (2017)

Bailly et al. (2017)

Kauke et al. (2016)

Sicard et al. (2015)

Loupy et al. (2013)

Studies

C4d

C1q

Overall

Subtotal (I-squared = 40.7%, p = 0.038)

Overall (I-squared = 29.5%, p = 0.056)

NOTE: Weights are from random effects analysis

Subtotal (I-squared = 29.8%, p = 0.240)

Population

Patients with

Non complement complement

activating DSA activating DSA

Patients

Without

DSA

Patients with

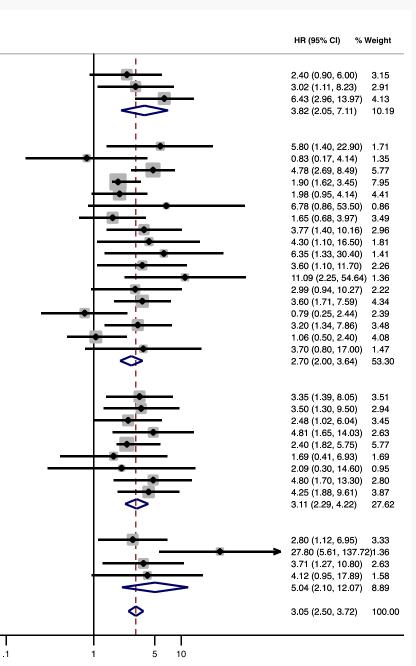




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lgG3				
Kaneku et al. (2012)	39	0	24	12
Freitas et al. (2013)	203	149	30	24
Everly et al. (2014)	179	132	22	25
Arnold et al. (2014)	274	180	20	74
O'Leary et al. (2015)	1270	1086	131	53
Khovanova et al. (201	5)80	0	45	35
Khovanova et al. (201	5)80	0	53	27
Lefaucheur et al. (201	6)125	0	90	35
Viglietti et al. (2017)	851	665	144	42
Subtotal (I-squared =	0.0%, p = 0	0.868)		
C3d				
Sicard et al. (2015)	69	0	29	40
Comoli et al. (2016)	114	0	105	9
Sicard et al. (2017)	52	0	31	21
Couchonnal et al (201	7)100	76	6	18
Subtotal (I-squared =	51.2%, p =	= 0.105)		

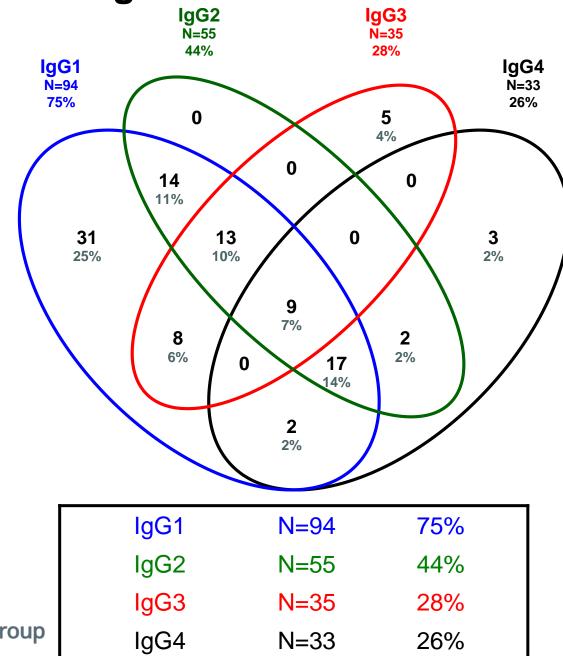


# Factors influencing complement fixing (CF) HLA-Ab in vitro (C1q reactivity)

- Presence of complement fixing (CF) IgG subtypes (IgG1/IgG3)
- 2. Level of IgG subtypes (weak /strong MFI)
- 3. Mixture of CF and non CF (NCF) (C1q reactivity)
- Impact of antibody removal therapy: Loss of C1q reactivity – diminished IgG subtype reactivity-NOT Switch of IgG subtype



# **DSA IgG subclass distribution**



 Paris Transplant Group

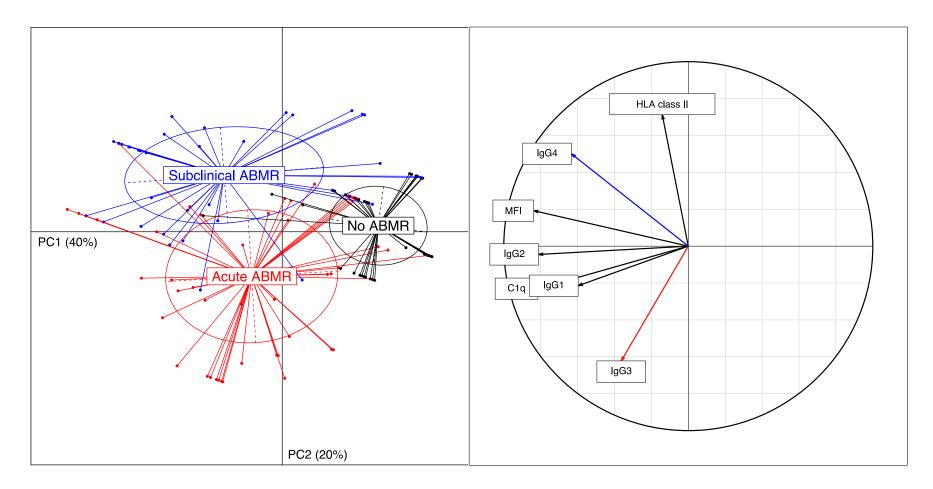
 Kidney, Heart & Lung

#### DSA IgG SUBCLASS COMPOSITION ACCORDING TO C1q STATUS

IgG subclass composition	All patients	C1q- DSA	C1q+ DSA
igo subciass composition	N=157	N=113	N=44
None	24 (15)	24 (21)	0
1	28 (18)	21 (19)	7 (16)
2	6 (4)	6 (5)	0
3	6 (4)	4 (4)	2 (5)
4	5 (3)	5 (4)	0
1+2	24 (15)	21 (19)	3 (7)
1+3	28 (18)	13 (12)	15 (34)
1+4	5 (3)	3 (3)	2 (5)
2+4	4 (3)	4 (4)	0
1+2+3	8 (5)	2 (2)	6 (14)
1+2+4	17 (11)	10 (9)	7 (16)
1+2+3+4	2 (1)	0	2 (5)

All C1q-binding DSAs were positive for IgG1 and/or IgG3 subtypes C1q negative DSA does not indicate absence of IgG1 or IgG3

# Identification of distinct patterns of injury according to DSA characteristics



1) IgG1-4, C1q and pan-IgG MFI segregate presence/absence of ABMR

2) IgG3 and IgG4 segragate ABMR phenotype

## IMMUNOLOGIC DETERMINANTS OF C1q POSITIVITY: MULTIVARIATE MODEL

DSA: N=157 C1q DSA: N=44

	OR	95%CI	Р
MFI level	1	[1.00-1.00]	<0.001
lgG1			
Νο	1		
Yes	5.59	[0.90-34.60]	0.064
lgG3			
Νο	1		
Yes	3.66	[1.40-9.54]	0.008

Univariate analysis considered: MFI level, HLA class, IgG1, IgG2, IgG3 and IgG4 subclasses

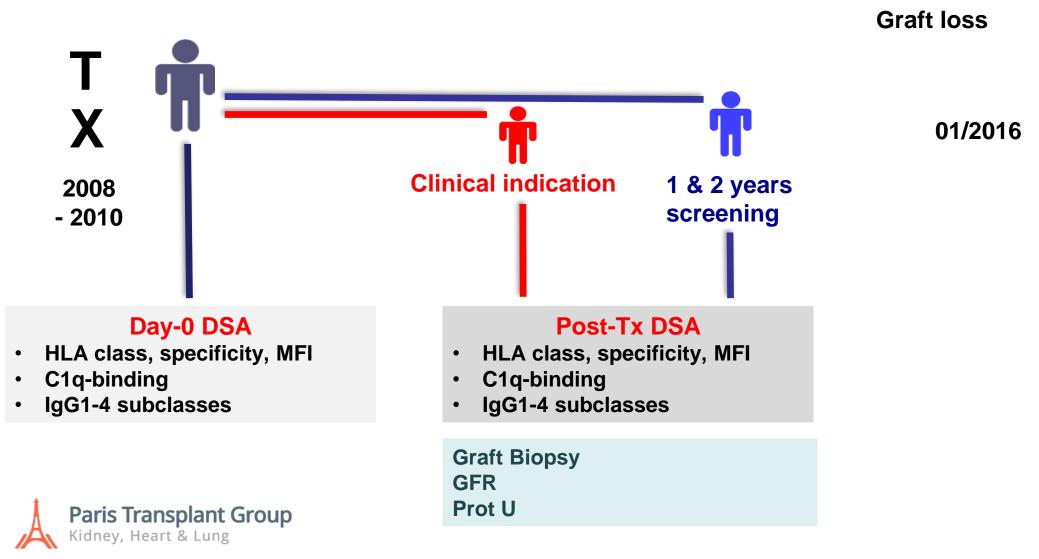


Systematic monitoring and characterization of DSA could add to the predictive value for allograft loss of the conventional approach based on their detection and strength

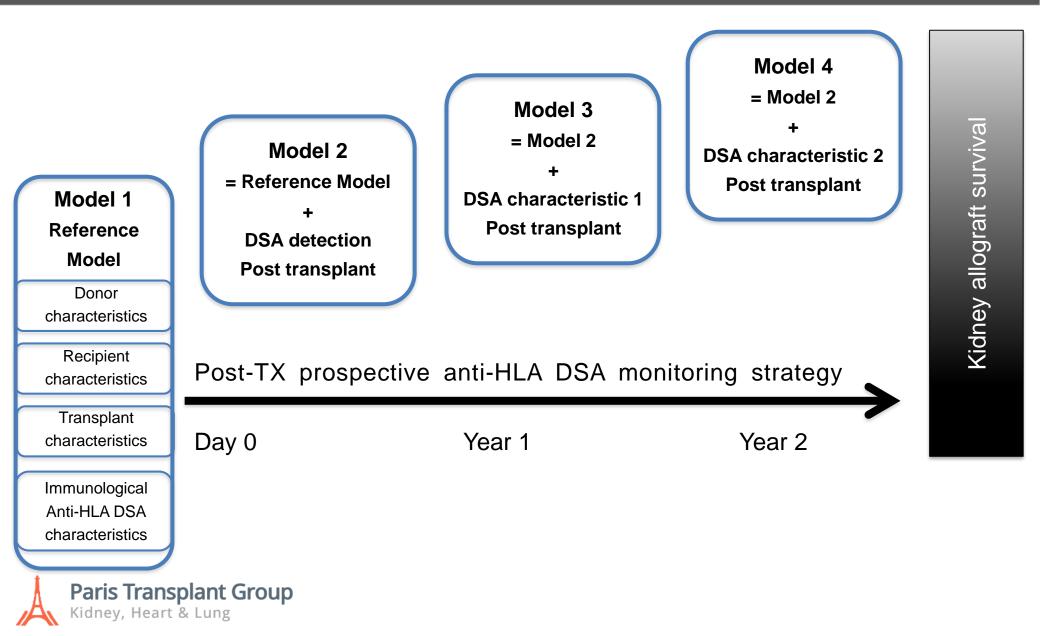


# **STUDY DESIGN**

**Prospective DSA monitoring strategy** 



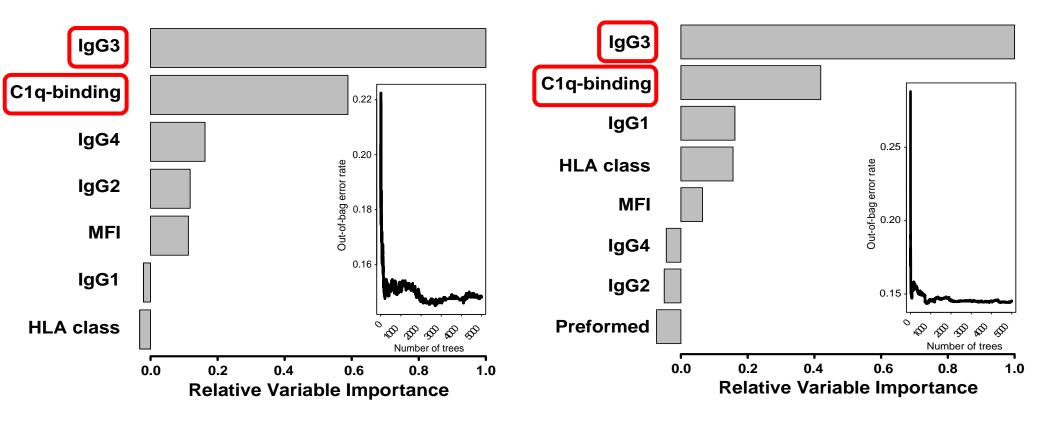
#### DYNAMIC MODELING TO ASSESS IMPROVEMENT IN RISK PREDICTION ACCORDING TO DSA MONITORING AND CHARACTERIZATION



#### Hierarchical ranking by multivariate survival random forest modeling

Day-0 (N=110)

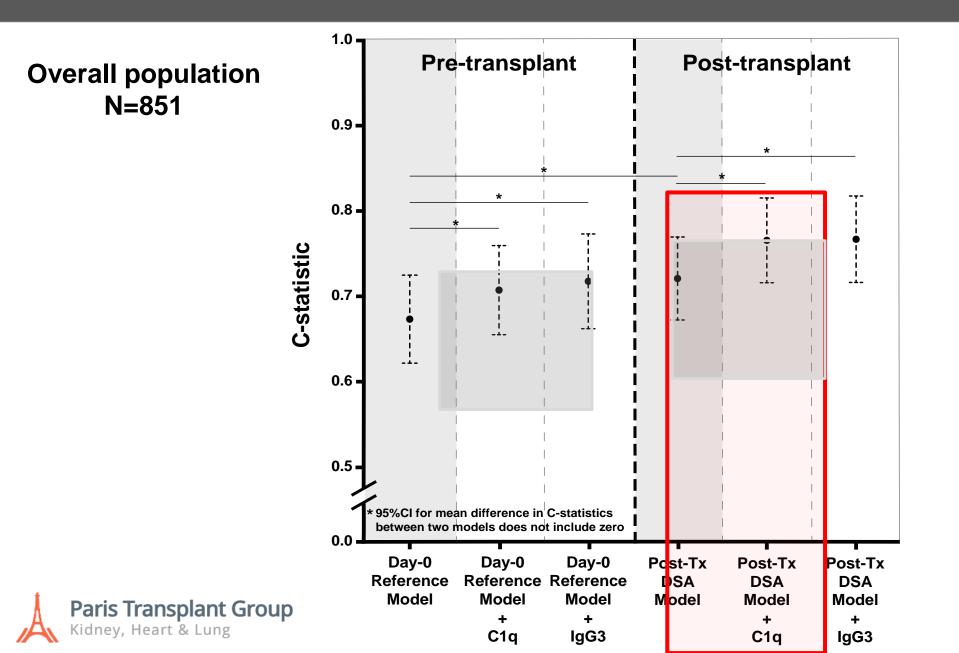
Post-Tx (N=186)





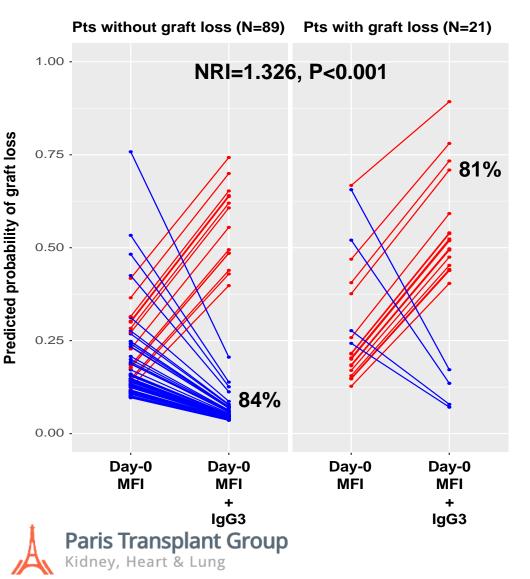
Viglietti D, JASN, 2016

#### PREDICTIVE VALUE OF DSA MONITORING AND CHARACTERIZATION



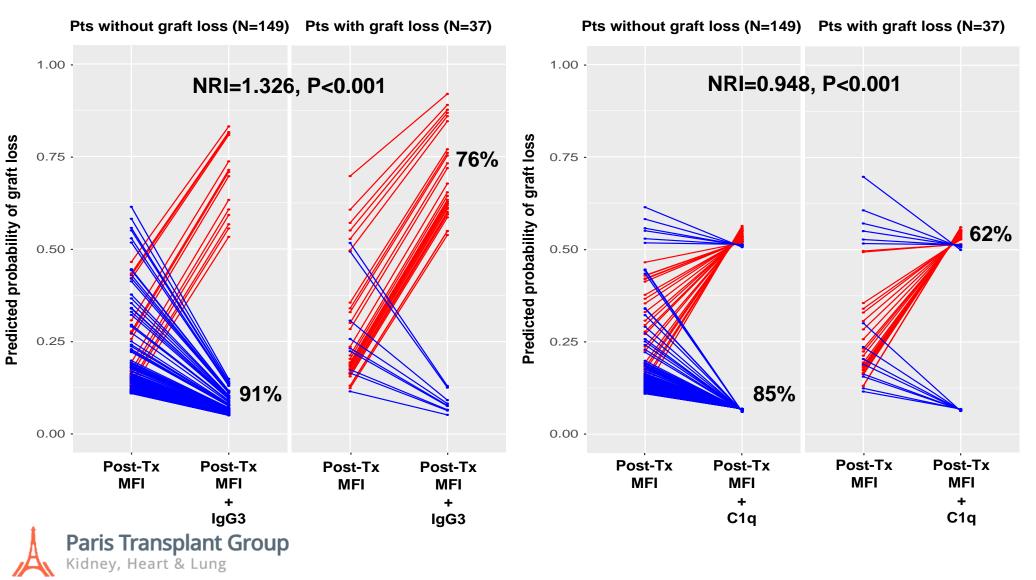
### **RISK RECLASSIFICATION BY IgG3 AND C1q BEYOND MFI**

#### In patients with Day-0 DSA



## **RISK RECLASSIFICATION BY IgG3 AND C1q BEYOND MFI**

#### In patients with Post-Tx DSA



CLINICAL RESEARCH www.jasn.org

#### Value of Donor–Specific Anti–HLA Antibody Monitoring and Characterization for Risk Stratification of Kidney Allograft Loss

Denis Viglietti,\*<sup>†</sup> Alexandre Loupy,<sup>†‡</sup> Dewi Vernerey,<sup>§</sup> Carol Bentlejewski,<sup>∥</sup> Clément Gosset,<sup>¶</sup> Olivier Aubert,<sup>†</sup> Jean-Paul Duong van Huyen,\*\* Xavier Jouven,<sup>†</sup> Christophe Legendre,<sup>†‡</sup> Denis Glotz,\*<sup>†</sup> Adriana Zeevi,<sup>∥</sup> and Carmen Lefaucheur\*<sup>†</sup>

- Prospective, systematic monitoring of DSA improved risk stratification for allograft loss beyond traditional determinants
- IgG3 positivity and C1q-binding capacity were the most informative DSA characteristics for classifying patients according to their risk of allograft loss
- IgG3 positivity or C1q-binding capacity improved risk stratification at the population level and also in patients with DSA beyond MFI level
- Further studies are needed to determine the most cost efficient DSA screening policies





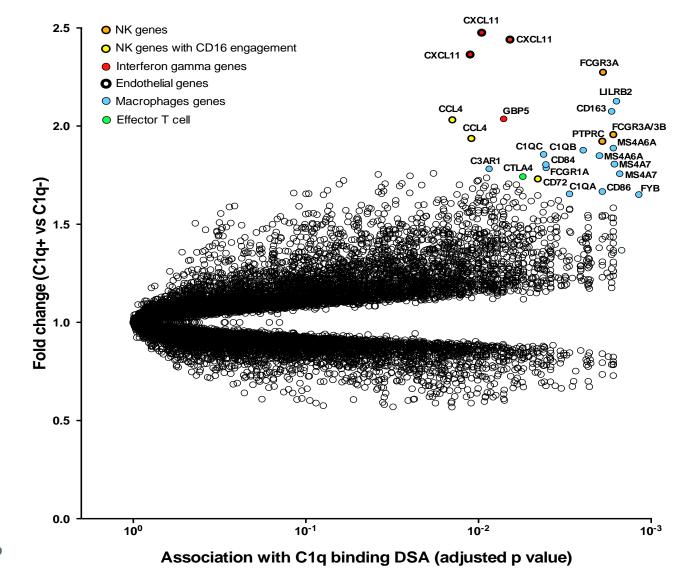
### Complement binding capacity

IgG subclass composition



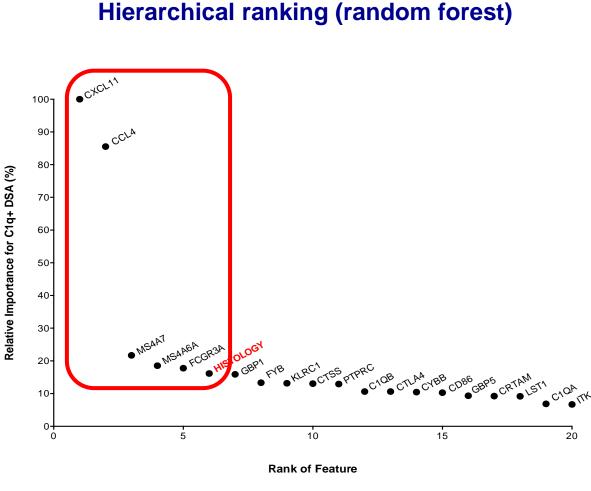
# INTRAGRAFT GENE EXPRESSION ACCORDING TO DSA C1q STATUS

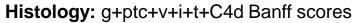
#### 9954 IQR-filtered genes

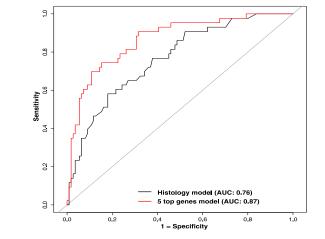


**Paris Transplant Group** Kidney, Heart & Lung

### RELATIVE IMPORTANCE OF C1q SELECTIVE GENES AND HISTOLOGY IN DETERMINING DSA C1q STATUS







Top genes	<b>Biological association</b>
CXCL11	ENDOTHELIAL IFNG RESPONSE
CCL4	NK CELL CD16- ENGAGEMENT/MACROPHAGE IFNG RESPONSE
MS4A6A	MONOCYTE/MACROPHAGE
MS4A7	MONOCYTE/MACROPHAGE
FCGR3A	NK CELL



#### BIOLOGICAL RELEVANCE OF C1q DSA TRANSCRIPTS

#### Human rejection effector cells culture

CCL4         0.13         0.44         0.44         0.42         0.44         0.01         0.35         3.13         0.46         0.43         3.13           CCL4         0.17         0.03         0.32         0.33         -0.33         -0.32         0.22         0.33         -0.33         0.32         0.22         0.33         -0.33         0.32         0.22         0.33         0.32         0.22         0.33         0.32         0.22         0.33         0.32         0.33         0.32         0.33         0.32         0.33         0.32         0.32         0.33         0.32         0.33         0.32         0.33         0.32         0.33         0.32         0.33         0.32         0.31         0.71         0.37         0.37         0.37         0.33         0.32         0.33         0.39         0.33         0.32         0.33         0.32         0.33         0.32         0.33         0.32         0.33         0.34         0.34         0.34         0.34         0.33         0.32         0.33         0.32         0.33         0.33         0.33         0.33         0.33         0.33         0.33         0.33         0.33         0.33         0.33         0.33 <t< th=""><th></th><th>Gene Symbol</th><th>Control Kidney</th><th>CD4</th><th>CD8</th><th>NK Unstimulated</th><th>NK CD16- Stimulated</th><th>B cell</th><th>Monocyte</th><th>Macrophage unstim</th><th>Macrophage + IFNG</th><th>HUVEC</th><th>HUVEC + IFNG</th><th>Avg signal</th></t<>		Gene Symbol	Control Kidney	CD4	CD8	NK Unstimulated	NK CD16- Stimulated	B cell	Monocyte	Macrophage unstim	Macrophage + IFNG	HUVEC	HUVEC + IFNG	Avg signal
CCL4 C102 C102 C102 C102 C102 C102 C102 C102		AIM2	-0.66	0.06	-0.03	-0.55	-0.53	2.00	0.43	-0.33	2.23	-0.67	-0.60	162
CCL4         -0.18         -0.33         -0.33         -0.33         -0.32         0.22         3.29         -0.34         -0.34           CCL4         -0.57         -0.34         -0.07         0.02         -0.51         -0.69         1.56         1.53         1.98         -0.71         -0.71         -4.71           CCL4         -0.55         -0.35         0.048         -0.48         -0.48         -0.48         -0.22         -2.71         1.36         -0.44         -0.37         0.71         -0.57         -0.57         -0.57         -0.72         -0.40         -0.32         -0.44         -0.44         -0.48         -0.48         -0.48         -0.48         -0.40         -0.31         0.71         -0.57         -0.57         -0.60         -0.21         -0.32         -0.34         -0.40         -0.31         -0.55         -0.50         -0.21         -0.33         -0.56         -0.57         7         -0.55         -0.55         -0.21         -0.33         -0.24         -0.22         -0.29         -0.29         -0.29         -0.29         -0.29         -0.29         -0.29         -0.29         -0.29         -0.29         -0.29         -0.29         -0.29         -0.29         -0.29		C1QA	0.13	-0.44	-0.46	-0.44	-0.42	-0.44	0.01	0.35	3.13	-0.46	-0.43	208
CCL4       Can       -0.57       -0.34       -0.07       0.02       -0.51       -0.66       1.56       1.58       1.98       -0.71       -0.71       4         CCL4       Cols       -0.55       -0.53       -0.13       0.13       0.071       -0.57       -0.73       4         CD183       -0.48       -0.48       -0.48       -0.48       -0.48       -0.48       -0.40       -0.32       -0.34       -0.40       -0.71       4       4         CD2       -0.40       -0.35       -0.30       -0.33       -0.30       -0.32       -0.40       -0.32       -0.34       -0.40       -0.71       4       4       4       -0.40       -0.22       -0.27       -0.33       -0.30       -0.40       -0.32       -0.34       -0.40       -0.57       -0.50       -0.51       -0.61       1.58       -0.66       -0.57       7         CD84       -0.57       -0.52       -0.61       -0.53       -0.51       -0.61       -0.53       -0.40       -0.22       -0.22       -0.29       -0.27       -0.27       -0.23       -0.29       -0.27       -0.27       -0.24       -0.27       -0.24       -0.27       -0.24       -0.25       -0.16		C1QB	-0.17	-0.33	-0.31	-0.32	-0.31	-0.33	-0.25	0.04	3.31	-0.35	-0.33	318
CCL4       -0.55       -0.50       -0.33       0.13       0.71       -0.57       12         CD183       -0.48       -0.48       -0.48       -0.48       -0.48       -0.48       -0.48       -0.48       -0.48       -0.48       -0.48       -0.48       -0.48       -0.44       -0.44       -0.44       -0.44       -0.43       -0.44       -0.44       -0.42       -0.57       -0.42       -0.32       -0.40       -0.41       1.36       -0.48       -0.48       -0.48       -0.48       -0.48       -0.44       -0.32       -0.40       -0.41       1.40       -0.40       -0.41       1.48       -0.48       -0.48       -0.48       -0.48       -0.48       -0.40       -0.41       1.48       -0.48       -0.40       -0.41       1.48       -0.48       -0.48       -0.48       -0.40       -0.41       1.48       -0.48       -0.48       -0.48       -0.48       -0.40       -0.41       -0.33       -0.34       -0.40       -0.47       -0.27       -0.27       -0.24       -0.27       -0.27       -0.24       -0.27       -0.28       E       -0.48       -0.48       -0.48       -0.33       -0.34       -0.41       -0.43       -0.45       -0.44       -0.45			-0.18	-0.33	-0.32	-0.33	-0.33	-0.33	-0.32	0.22	3.29	-0.34	-0.34	394
CXCL11         -0.45         -0.48         -0.48         -0.48         -0.48         -0.48         -0.48         -0.48         -0.48         -0.48         -0.48         -0.48         -0.48         -0.48         -0.48         -0.48         -0.48         -0.48         -0.48         -0.48         -0.44         -0.40         -0.33         2.031         -0.23         -0.33         2.031         -0.24         -0.41         11           CD84         -0.57         -0.24         -0.21         -0.33         2.066         1.19         1.58         -0.58         -0.55         10           CRTAM         -0.40         2.85         1.48         -0.38         -0.38         -0.39         -0.40         4.0.29         -0.29         -0.27         -0.27         -0.27         -0.27         -0.27         -0.27         -0.27         -0.27         -0.27         -0.27         -0.27         -0.28         -0.61         1.53         1.48         -0.33         -0.33         -0.34         -0.34         -0.34         -0.34         -0.34         -0.34         -0.34         -0.34         -0.34         -0.34         -0.34         -0.34         -0.34         -0.34         -0.34         -0.34         -0.34         -0.34		C3AR1	-0.57	-0.34	-0.07	0.02		-0.69	1.56	1.53	1.98	-0.71	-0.71	458
CXCL11         -0.45         -0.48         -0.48         -0.48         -0.48         -0.48         -0.48         -0.48         -0.48         -0.48         -0.48         -0.48         -0.48         -0.48         -0.48         -0.48         -0.48         -0.48         -0.48         -0.48         -0.44         -0.40         -0.33         2.031         -0.23         -0.33         2.031         -0.24         -0.41         11           CD84         -0.57         -0.24         -0.21         -0.33         2.066         1.19         1.58         -0.56         -0.55         -0.62         -0.62         -0.27         -0.24         -0.29         -0.29         -0.29         -0.27         -0.24         -0.29         -0.29         -0.27         -0.72         -0.74         -0.53         -0.33 <th>CCI 4</th> <th>CCL4</th> <th>-0.55</th> <th>-0.50</th> <th>0.03</th> <th>0.60</th> <th>2.95</th> <th>-0.56</th> <th>-0.53</th> <th>0.13</th> <th>0.71</th> <th>-0.57</th> <th>-0.57</th> <th>1258</th>	CCI 4	CCL4	-0.55	-0.50	0.03	0.60	2.95	-0.56	-0.53	0.13	0.71	-0.57	-0.57	1258
CXCL11         0.57         0.24         0.23         0.055         0.08         0.21         0.33         2.66         1.58         0.056         0.056         1.65         0.18         0.08         2.30           CXCL11         0.454         0.55         0.42         0.57         0.52         0.08         2.36         1.16         1.58         -0.58         0.61         1.16         0.27         0.22         -0	UULI	CD163	-0.45	-0.48	-0.48	-0.48	-0.48	-0.48	0.72	2.71	1.36	-0.48	-0.48	641
CXCL11         Cost         -0.54         -0.67         -0.62         -0.08         2.36         1.19         1.50         -0.58         -0.56         1.10           CTLA4         -0.29         -0.27         -0.27         -0.29         -0.27         -0.29         -0.27         -0.29         -0.27         -0.24         -0.22         -0.29         -0.27         -0.24         -0.29         -0.27         -0.24         -0.29         -0.27         -0.24         -0.29         -0.27         -0.24         -0.25         -0.21         -0.25         -0.25         -0.23         -0.39         -0.40         -0.28         -0.07         3.33         -0.34         -0.34         -0.34         -0.34         -0.34         -0.34         -0.34         -0.34         -0.34         -0.34         -0.34         -0.34         -0.34         -0.34         -0.34         -0.34         -0.34         -0.33         -0.34         -0.34         -0.34         -0.33         -0.34         -0.34         -0.34         -0.33         -0.34         -0.33         -0.34         -0.33         -0.34         -0.33         -0.34         -0.33         -0.34         -0.33         -0.34         -0.33         -0.34         -0.34         -0.33         -0.24 <th></th> <td>CD72</td> <td>-0.40</td> <td>-0.35</td> <td>-0.30</td> <td>-0.33</td> <td>3.09</td> <td>0.97</td> <td>-0.40</td> <td>-0.32</td> <td>-0.34</td> <td>-0.40</td> <td>-0.41</td> <td>137</td>		CD72	-0.40	-0.35	-0.30	-0.33	3.09	0.97	-0.40	-0.32	-0.34	-0.40	-0.41	137
CRTAM       -0.29       -0.27       -0.27       3.33       -0.29       -0.27       -0.24       -0.22       -0.29		CD84	-0.57	-0.24	-0.23	-0.55	-0.50	-0.21	0.33	2.66	1.58	-0.56	-0.57	706
CXCL11         CTLA4         -0.40         2.85         1.48         -0.38         -0.38         -0.39         -0.40         -0.39         -0.40         -0.40         -0.40         -0.40         -0.55           CXCL11         -0.58         -0.61         -0.53         -0.16         1.53         1.87         1.75         -0.72         -0.07         37           CXCL11         -0.53         -0.34         -0.33         -0.34         -0.33         -0.44         -0.46         1.49         -0.35         1.49         -0.63         -0.33         -0.44         -0.33         -0.44         -0.33         -0.34         -0.34         -0.34		CD86		-0.55	-0.42	-0.57	-0.52	-0.08	2.36		1.50	-0.58	-0.55	103
CXCL11       -0.58       -0.61       -0.50       -0.55       -0.16       1.53       1.87       1.75       -0.72       -0.07       37         CXCL11       -0.34       -0.34       -0.34       -0.33       -0.33       -0.34       -0.13       -0.34       -3.28       7         CYBB       -0.34       -0.46       1.49       -0.66       2.93       1.08       0.49       -0.54       -0.46       1.66       1.29       -0.34       <		CRTAM	-0.29	-0.29	-0.27	-0.27	3.33	-0.29	-0.27	-	-0.22	-0.29	-0.29	85
CXCL11       -0.34       -0.34       -0.35       -0.33       -0.35       -0.34       -0.34       -0.34       -0.34       3.28       7/4         CYBE       -0.53       -0.53       -0.53       -0.53       -0.35       -0.34       -0.35       1.49       0.063       0.035       3.29       -0.34       -0.34       -0.34       -0.34       -0.34       -0.34       -0.34       -0.35       1.49       0.063       0.055       0.12       -0.57       3       -0.56       -0.17       -0.11       -0.64       1.24       -0.64       1.29								-0.39	-0.40		-0.39			80
CYBB       -0.53       -0.54       -0.53       -0.53       -0.33       2.28       1.43       1.44       -0.54       -0.54       1.25         EMR2       -0.46       -0.45       -0.44       -0.45       -0.44       -0.45       2.03       1.08       0.49       -0.45       -0.46       1.6         EVI2A       -1.06       0.96       0.48       0.31       1.49       -0.33       1.43       0.63       0.33       -1.05       -0.66       9.7         FCGR1A///FCGR1B///FCGR1C       -0.34       -0.34       -0.34       -0.33       -0.34       0.05       0.05       3.29       -0.34       -0.37       -0.57       3         FCGR1A///FCGR3B       -0.49       -0.50       -0.44       -0.64       -0.64       -0.64       -0.64       -0.64       -0.66       -0.31       -0.09       -0.64       -0.76       -0.81       0.09       0.26       -0.12       -0.71       -0.46       1.44         FGR3A       FGR3A       FGR3A       FGR3A       FGGR3A       -0.69       -0.64       -0.26       -0.81       0.09       0.26       -0.12       -0.71       -0.46       1.24         FGB3A       FGB3       -0.65       0.95		CTSS	-0.72	-0.58	-0.61					1.87	1.75	-0.72		3789
CYBB       -0.53       -0.54       -0.53       -0.53       -0.33       2.28       1.43       1.44       -0.54       -0.54       1.25         EMR2       -0.46       -0.45       -0.44       -0.45       -0.44       -0.45       2.03       1.08       0.49       -0.45       -0.46       1.6         EVI2A       -1.06       0.96       0.48       0.31       1.49       -0.33       1.43       0.63       0.33       -1.05       -0.66       9.7         FCGR1A///FCGR1B///FCGR1C       -0.34       -0.34       -0.34       -0.33       -0.34       0.05       0.05       3.29       -0.34       -0.37       -0.57       3         FCGR1A///FCGR3B       -0.49       -0.50       -0.44       -0.64       -0.64       -0.64       -0.64       -0.64       -0.66       -0.31       -0.09       -0.64       -0.76       -0.81       0.09       0.26       -0.12       -0.71       -0.46       1.44         FGR3A       FGR3A       FGR3A       FGR3A       FGGR3A       -0.69       -0.64       -0.26       -0.81       0.09       0.26       -0.12       -0.71       -0.46       1.24         FGB3A       FGB3       -0.65       0.95	CXCL11	CXCL11	-0.34	-0.34	-0.34	-0.35	-0.33	-0.35	-0.34	-0.34	-0.13	-0.34	3.28	708
FCGR3A       -1.06       0.96       0.48       0.31       1.49       -0.35       1.49       0.63       0.33       -1.05       -1.06       9         FCGR1A///FCGR1B///FCGR1B       -0.34       -0.34       -0.34       -0.33       -0.34       0.05       0.05       3.29       -0.34       -0.34       -0.34       5         FCGR1A///FCGR1B       -0.49       -0.50       -0.47       -0.50       -0.48       1.66       1.66       1.92       -0.57       -3         FCGR3A///FCGR3B       -0.49       -0.55       -0.47       -0.50       -0.48       1.06       1.66       1.92       -0.57       -3         FKBP5       -0.39       -0.48       -0.69       -0.64       -0.26       -0.81       0.09       0.26       -0.12       -0.71       -0.46       1.46         GBP5       -0.65       0.95       1.35       0.26       -0.59       -0.87       1.93       0.41       0.79       -0.84       -0.78       2.1         GBP5       -0.78       0.01       -0.26       0.54       0.13       -0.77       -0.63       -0.72       2.72       -0.78       0.88       1.14       1.08       1.18       1.17       -0.63       -0	••••	САВВ				-0.53	-0.53				1.44		-0.54	1260
FCGR1A///FCGR1B///FCGR1C       -0.34       -0.34       -0.34       -0.33       -0.34       0.05       3.29       -0.34       -0.34       5         FCGR3A///FCGR3B       -0.49       -0.56       -0.56       -0.47       -0.50       -0.48       1.66       1.92       -0.57       -0.55       -0.12       -0.12       -0.12       -0.12       -0.12       -0.18       -0.02       -0.57       -0.58       -0.55       -				-0.45	-0.45	-0.44	-0.45		2.93	1.08	0.49	-0.45	-0.46	136
FCGR3A       -0.49       -0.56       -0.47       -0.50       -0.48       1.66       1.66       1.92       -0.57       -0.57       3         FCGR3A///FCGR3B       -0.49       -0.50       -0.49       2.32       2.12       -0.49       0.06       -0.31       -0.24       -0.50       -0.57       3         FKBP5       -0.39       -0.48       -0.69       -0.64       -0.26       -0.31       0.026       -0.12       -0.71       -0.46       1.44         GBP1       -0.65       -0.36       -0.56       -0.35       -0.30       -0.70       -0.41       -0.30       1.96       -0.66       2.08       1.66         GBP5       -0.78       0.01       -0.26       0.54       0.13       -0.74       -0.63       -0.72       2.72       -0.78       0.88       100         ILTR       -0.64       2.72       0.33       -0.19       -0.03       -0.63       -0.64       1.29       0.24       -0.60       -0.53       -0.63       -0.65       1.14       -1.08       0.11       8         ILTR       -0.64       2.72       0.33       -0.52       -0.53       -0.52       -0.63       -0.63       -0.63       -0.63 <th< th=""><th></th><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td>0.33</td><td></td><td></td><td>974</td></th<>											0.33			974
FCGR3A///FCGR3B       -0.49       -0.50       -0.49       2.32       2.12       -0.49       0.06       -0.31       -0.24       -0.50       -0.50       6         FKBP5       -0.39       -0.48       -0.69       -0.64       -0.26       -0.81       0.09       0.26       -0.12       -0.71       -0.46       14         FYB       -0.85       0.95       1.35       0.26       -0.59       -0.87       1.93       0.41       0.79       -0.84       -0.78       22         GBP1       -0.65       -0.36       -0.56       -0.45       -0.03       -0.70       -0.41       -0.30       1.96       -0.66       2.08       18         GBP5       -0.78       0.01       -0.26       0.54       0.13       -0.74       -0.63       -0.72       2.72       -0.78       0.88       10         IL7R       -0.64       2.72       0.33       -0.19       -0.03       -0.63 <t< th=""><th></th><td></td><td></td><td></td><td></td><td>-0.34</td><td>-0.33</td><td></td><td></td><td></td><td></td><td></td><td></td><td>553</td></t<>						-0.34	-0.33							553
FKBP5       -0.39       -0.48       -0.69       -0.64       -0.26       -0.81       0.09       0.26       -0.12       -0.71       -0.46       14         FYB       -0.85       0.95       1.35       0.26       -0.59       -0.87       1.93       0.41       0.79       -0.84       -0.78       2.08         GBP1       -0.65       -0.36       -0.56       -0.45       -0.30       -0.70       -0.41       -0.30       1.96       -0.66       2.08       1.8         GBP5       -0.78       0.01       -0.26       0.54       0.13       -0.74       -0.63       -0.72       2.72       -0.78       0.88       10         IL7R       -0.64       2.72       0.33       -0.19       -0.063       -0.63       -0.63       -0.64       -0.64       -0.64       0.13       -0.64       -0.65       1.14       -1.08       0.11       8         IS20       -1.16       0.59       1.43       -0.18       0.25       1.75       -0.96       -0.63       -0.63       -0.63       -0.63       -0.63       -0.63       -0.63       -0.63       -0.63       -0.63       -0.63       -0.63       -0.63       -0.63       -0.63       -0.63 <th></th> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td>1.66</td> <td></td> <td></td> <td></td> <td></td> <td>389</td>									1.66					389
FKBPS       -0.39       -0.48       -0.69       -0.64       -0.26       -0.81       0.09       0.26       -0.12       -0.71       -0.74       10.71       -0.76       12         FYB       -0.85       0.95       1.35       0.26       -0.59       -0.87       1.93       0.41       0.79       -0.84       -0.78       2.08         GBP1       -0.65       -0.36       -0.56       -0.41       -0.74       -0.63       -0.72       2.72       -0.78       0.88       100         GBP5       -0.78       0.01       -0.26       0.54       0.13       -0.74       -0.63       -0.72       2.72       -0.78       0.88       100         IL7R       -0.64       2.72       0.33       -0.19       -0.03       -0.63       -0.65       1.14       -1.08       0.11       8         ISG20       -1.16       0.59       1.43       -0.18       0.25       1.75       -0.96       -0.63       -0.63       -0.63       -0.63       -0.63       -0.63       -0.63       -0.63       -0.63       -0.63       -0.63       -0.63       -0.63       -0.63       -0.63       -0.63       -0.63       -0.52       1.93       3.02       0.48	FCGR3A		-0.49	-0.50	-0.49	2.32	2.12	-0.49	0.06	-0.31	-0.24	-0.50	-0.50	642
GBP1         -0.65         -0.36         -0.56         -0.45         -0.30         -0.70         -0.41         -0.30         1.96         -0.66         2.08         18           GBP5         -0.78         0.01         -0.26         0.54         0.13         -0.74         -0.63         -0.72         2.72         -0.78         0.88         10           IL7R         -0.64         2.72         0.33         -0.19         -0.03         -0.63         -0.64         1.29         0.24         -0.60         -0.54         5           ISG20         -1.16         0.59         1.43         -0.18         0.25         1.75         -0.96         -0.63         -0.53				-0.48		-0.64			0.09		-0.12			1494
GBP5         -0.78         0.01         -0.26         0.54         0.13         -0.74         -0.63         -0.72         2.72         -0.78         0.88         10           IL7R         -0.64         2.72         0.33         -0.19         -0.03         -0.63         -0.64         1.29         0.24         -0.60         -0.54         5           ISG20         -1.16         0.59         1.43         -0.18         0.25         1.75         -0.96         -0.63<						0.26		-0.87	1.93		0.79		-0.78	208
IL7R       -0.64       2.72       0.33       -0.19       -0.03       -0.63       -0.64       1.29       0.24       -0.60       -0.54       5         ISG20       -1.16       0.59       1.43       -0.18       0.25       1.75       -0.96       -0.63														1884
MS\$4A66       -0.39       -0.41       -0.45       1.75       -0.96       -0.65       1.14       -1.08       0.11       8         MS\$4A66       -0.63       1.38       1.08       1.24       1.96       -0.63       -0.64       -0.40       -0.40       -0.40       -0.40       -0.40       -0.40       -0.40       -0.41       -0.51       -0.31       -0.31       -0.31       -0.31       -0.31       -0.30       -0.32       -0.30       -0.41       1.1       1.5       -0.55       -0.44				0.01										1037
MS4A6A MS4A6A       -0.63       1.38       1.08       1.24       1.96       -0.63       -0.60       -0.40       -0.40       -0.40       -0.40       -0.40       -0.40       -0.40       -0.40       -0.40       -0.41       -0.41       -0.31       -0.31       -0.31       -0.31       -0.30       -0.32       -0.30       -0.31       1       -0.30       -0.40       -0.41       1       1       -0.66       -0.47       5											0.24			560
KLRC1///KLRC2       -0.40       -0.40       -0.24       1.34       2.92       -0.40       -0.41       -0.51       -0.52       1.79       1.60       1.86       -0.53       -0.53       -0.53       -0.53       -0.53       -0.53       -0.53       -0.53       -0.53       -0.53       -0.53       -0.53       -0.53       -0.53       -0.53       -0.53       -0.54       -0.51       -0.51       -0.51       -0.53       -0.54       -0.55       -0.53       -0.56				0.59			0.25				1.14		0.11	832
MS4A6A MS4A6A       -0.52       -0.53       -0.52       -0.53       -0.52       1.79       1.60       1.86       -0.53       -0.53       3         MS4A6A MS4A6A       -0.49       -0.25       -0.21       -0.45       -0.46       -0.43       3.02       0.48       0.83       -0.51       -0.50       5.5         MS4A6A MS4A6A       -0.36       -0.41       -0.41       -0.41       -0.41       -0.41       -0.30       -0.32       -0.30       -0.31       1         MS4A4A       -0.36       -0.41       -0.41       -0.41       -0.41       0.23       3.14       0.67       -0.41       -0.41       1         MS4A4A       -0.36       -0.41       -0.41       -0.45       -0.45       -0.47       2.92       0.84       0.83       -0.46       -0.47       5         MS4A7       -0.44       -0.51       -0.51       -0.51       -0.45       -0.47       2.92       0.84       0.83       -0.46       -0.47       5         PRKCB       -0.66       -0.03       0.40       0.33       -0.51       -0.59       2.70       1.29       0.82       -0.51       -0.51       -0.55       -0.53       -0.67       1.06       1.4 <th></th> <th>455</th>														455
MS4A6A MS4A6A         -0.49         -0.25         -0.21         -0.45         -0.46         -0.43         3.02         0.48         0.83         -0.51         -0.50         5.5           MS4A6A MS4A6A         -0.27         -0.29         -0.30         -0.31         -0.31         -0.31         -0.30         -0.32         -0.30         -0.31         1           MS4A4A         -0.36         -0.41         -0.41         -0.41         -0.41         0.23         3.14         0.67         -0.41         -0.41         1           MS4A4A         -0.39         -0.47         -0.47         -0.45         -0.45         -0.47         2.92         0.84         0.83         -0.46         -0.47         5           MS4A7         -0.44         -0.51         -0.51         -0.51         -0.29         2.70         1.29         0.82         -0.51         -0.51         -0.55         -0.55         -0.55         -0.55         -0.56         -0.66         1.4           PRKCB         -0.66         -0.03         0.40         0.33         -0.32         2.59         1.45         -0.55         -0.56         -0.66         -0.67         1.4														309
MEGF11       -0.27       -0.29       -0.30       -0.31       -0.31       -0.31       -0.30       -0.32       -0.30       -0.31       1         MS4A6A MS4A6A       -0.36       -0.41       -0.41       -0.41       -0.41       -0.41       0.23       3.14       0.67       -0.41       -0.41       1         MS4A6A       -0.39       -0.47       -0.47       -0.45       -0.45       -0.47       2.92       0.84       0.83       -0.46       -0.47       5         MS4A7       -0.44       -0.51       -0.51       -0.51       -0.29       2.70       1.29       0.82       -0.51       -0.51       5         PRKCB       -0.66       -0.03       0.40       0.33       -0.32       2.59       1.45       -0.55       -0.57       -0.67       1.49         PTPRC       -1.03       0.44       0.14       1.51       1.63       0.44       1.05       0.07       -0.02       -1.06       -1.06       1.45														354
MS4A4A       -0.36       -0.41       -0.41       -0.41       -0.41       0.23       3.14       0.67       -0.41       1         MS4A6A       -0.39       -0.47       -0.47       -0.45       -0.45       -0.47       2.92       0.84       0.83       -0.46       -0.47       55         MS4A7       -0.44       -0.51       -0.51       -0.51       -0.51       -0.29       2.70       1.29       0.82       -0.51       -0.51       55         PRKCB       -0.66       -0.03       0.40       0.33       -0.32       2.59       1.45       -0.55       -0.53       -0.67       1.46       1.06       1.46       1.06       1.46       1.06       1.46														582
MS4A6A MS4A7       -0.39       -0.47       -0.47       -0.45       -0.47       2.92       0.84       0.83       -0.46       -0.47       55         PRKCB       -0.66       -0.03       0.40       0.33       -0.51       -0.29       2.70       1.29       0.82       -0.51       -0.51       6         PTPRC       -1.03       0.44       0.14       1.51       1.63       0.44       1.05       0.07       -0.02       -1.06       -1.06       14														19
MS4A7         -0.44         -0.51         -0.51         -0.51         -0.29         2.70         1.29         0.82         -0.51         -0.51         -0.51           PRKCB         -0.66         -0.03         0.40         0.33         -0.32         2.59         1.45         -0.55         -0.53         -0.67         1           PTPRC         -1.03         0.44         0.14         1.51         1.63         0.44         1.05         0.07         -0.02         -1.06         -1.06         14			1											137
WIS4A1         PRKCB         -0.66         -0.03         0.40         0.33         -0.32         2.59         1.45         -0.55         -0.53         -0.67         1           PTPRC         -1.03         0.44         0.14         1.51         1.63         0.44         1.05         0.07         -0.02         -1.06         -1.06         14	IVIJ4A0A	MS4A6A	-0.39	-0.47	-0.47	-0.45	-0.45	-0.47		0.84	0.83	-0.46	-0.47	502
PTPRC         -1.03         0.44         0.14         1.51         1.63         0.44         1.05         0.07         -0.02         -1.06         -1.06         14	MS4A7		-0.44	-0.51	-0.51	-0.51						-0.51		632
														178
				-							-0.02			1473
Paris Transplant Group	Paris Transplant Group	SOD2	-0.43	-0.97	-1.03	-0.95	-0.76	-0.40	1.54	-0.04	0.41	-0.95	0.62	287

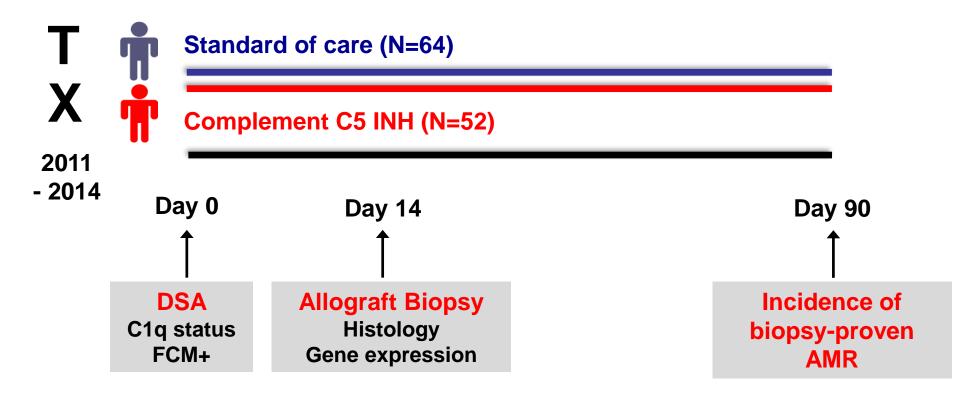
Paris Transplant Group Kidney, Heart & Lung

# Anti-HLA DSA characteristics & gene expression to identify responders to Eculizumab therapy



#### THERAPEUTIC STUDY: EFFECT OF COMPLEMENT INHIBITION

Multi-center, international study in HLA incompatible kidney recipients 11 centers in the US and Europe: NCT01567085 & NCT01399593

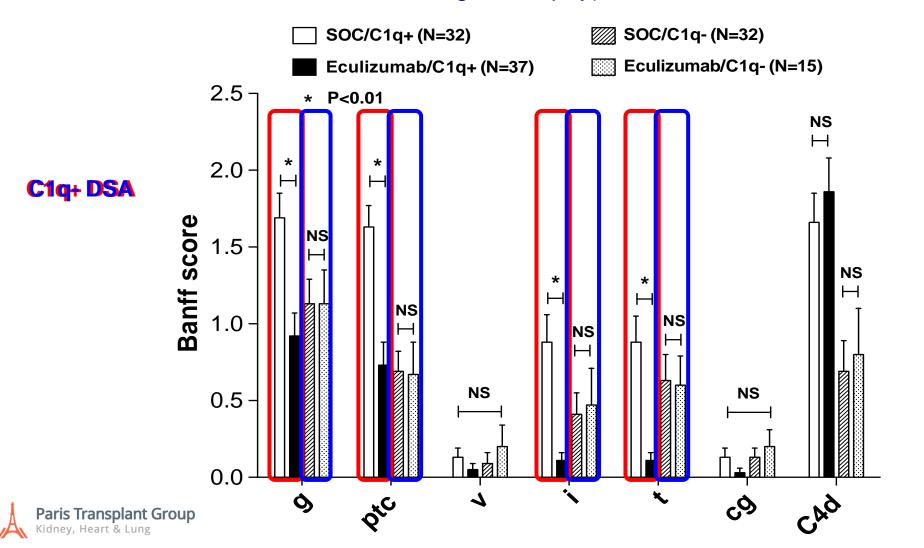


Standard of care: PE and IVIG according to local centers' protocol C5 INH: Eculizumab 1200 mg at Tx, 900 mg/week x4 and 1200 mg at week 5, 7, 9



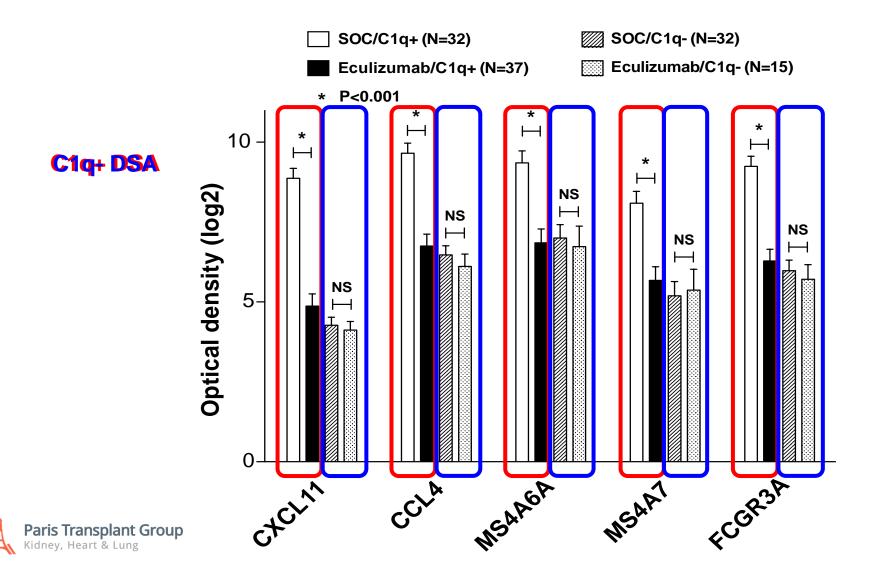
## EFFECT OF COMPLEMENT INHIBITION ON HISTOLOGY

Eculizumab specifically decreased acute injury in C1q+DSA patients (Day 14 allograft biopsy)



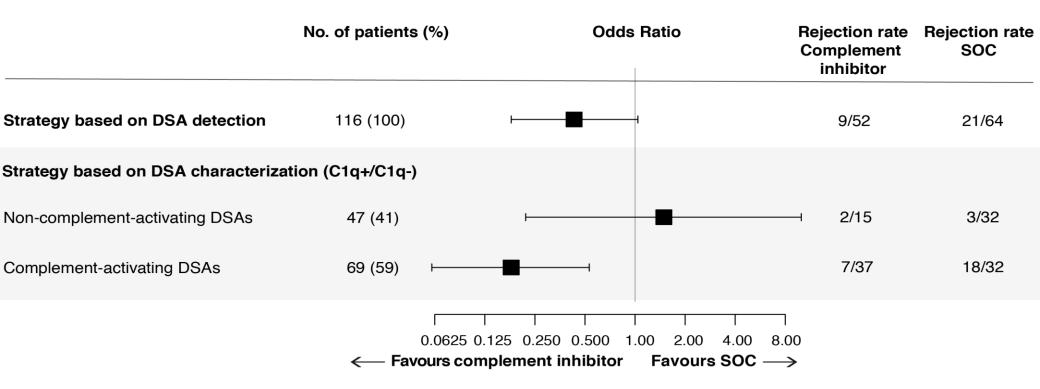
#### EFFECT OF COMPLEMENT INHIBITION ON THE C1q DSA GENE SET

#### Eculizumab specifically decreased the C1q gene set expression



# IMPACT OF A THERAPEUTIC STRATEGY BASED ON DSA C1q STATUS vs. DSA DETECTION

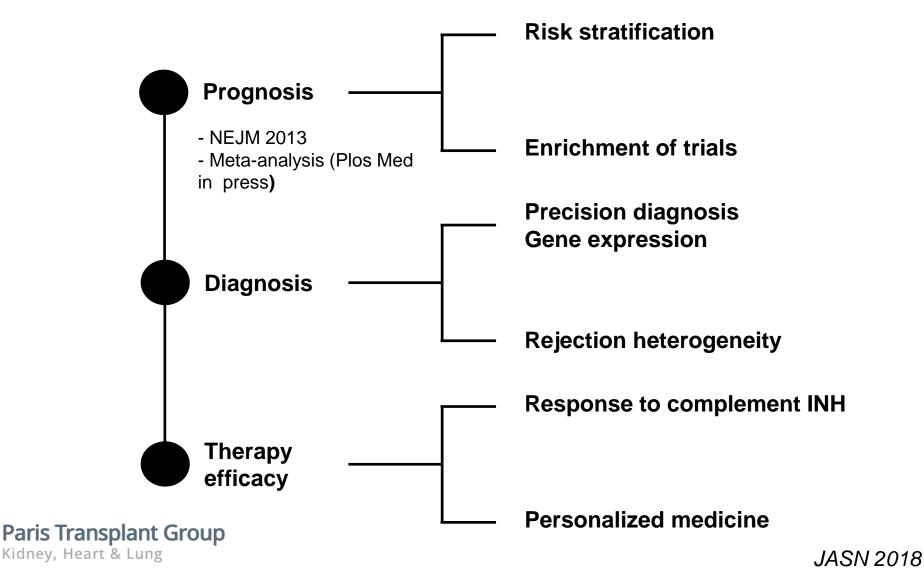
# Response rate to complement inhibition improved when characterizing DSA C1q status at transplantation





#### CONCLUSION

C'-binding HLA DSA as a biomarker in the era of new technologies



#### CONCLUSION

p < 0.0001

Nabs-

DSA+

Nabs-

DSA+

Nabs-

DSA+

Nabs-

DSA+

Proteinuria

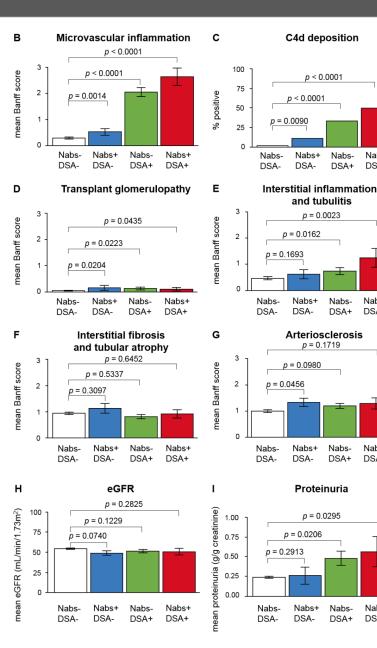
p = 0.0295

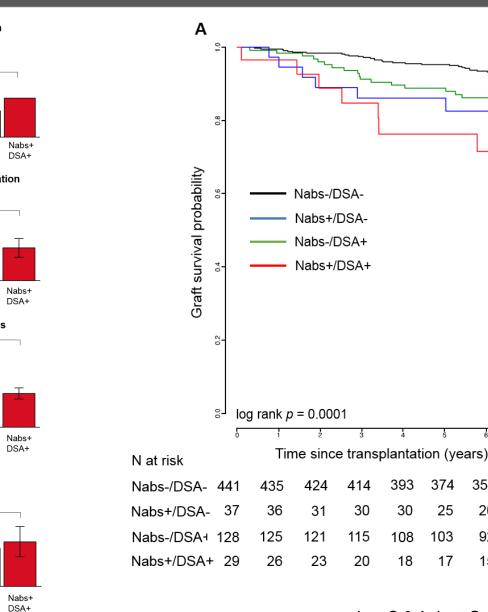
p = 0.1719

Nabs+

p = 0.0023

DSA-





#### Lee S & Aubert O et al. JASN in press

354

20

92

15

329

19

81

12

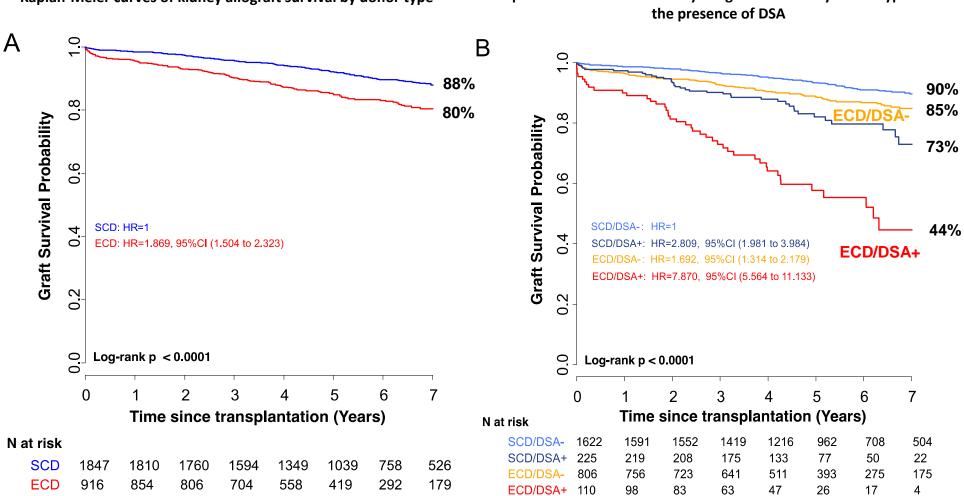
374

25

103

17

#### CONCLUSION



Kaplan-Meier curves of kidney allograft survival by donor type

Paris Transplant Group

Kidney, Heart & Lung

Kaplan-Meier curves of kidney allograft survival by donor type and

Aubert O et al. BMJ 2015

