



***REAL-LIFE CLINICAL IMPLEMENTATION OF A STRATEGY BASED ON CMV-SPECIFIC
CELL-MEDIATED IMMUNITY TO GUIDE CMV PREVENTIVE THERAPY IN SOLID
ORGAN TRANSPLANTATION***

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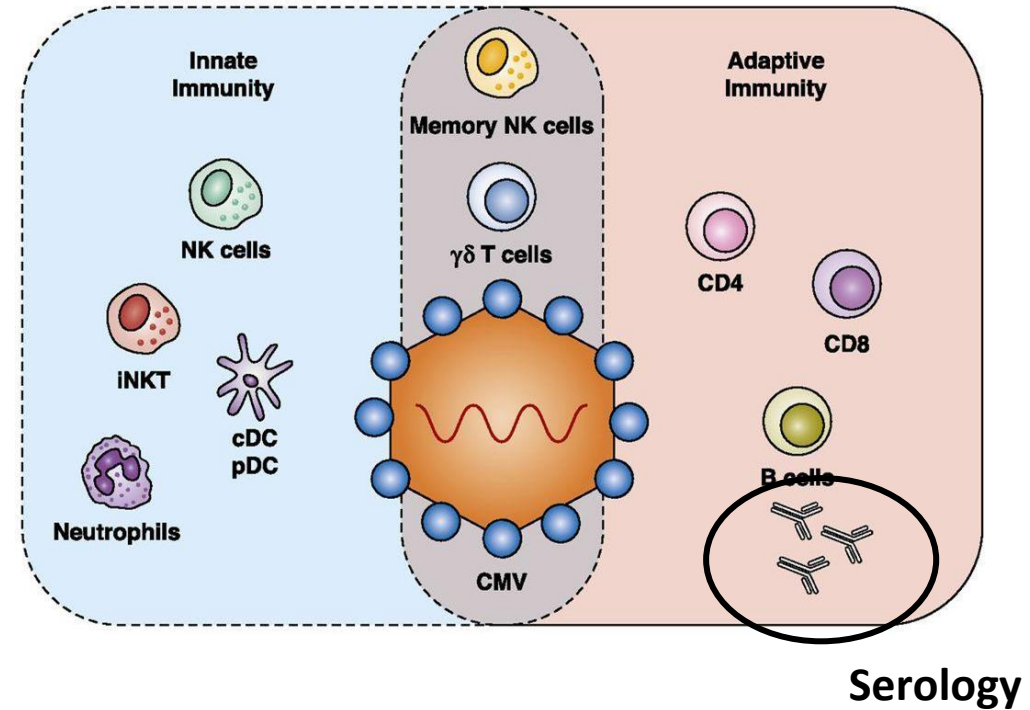
Context: CMV burden in SOT

Mortality/Graft survival/Rejection

Raval et al., Transplant Inf Dis 2021

Evaluation of the risk of CMV infection

Prophylaxis / preemptive strategies

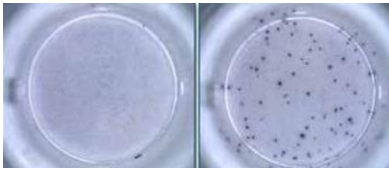
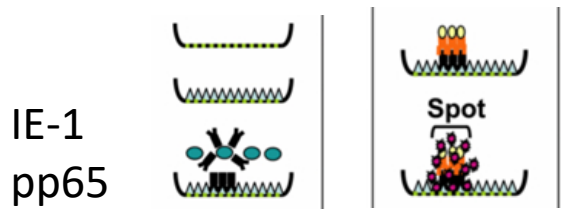


Picarda G, et al. J Immunol 2018

Need for more accurate tools to assess the risk of CMV infection and individualize preventive strategies

Context: CMV-Cell mediated immunity monitoring

T-SPOT[®].CMV



Count IFN- γ producing
T cells using ELISPOT reader

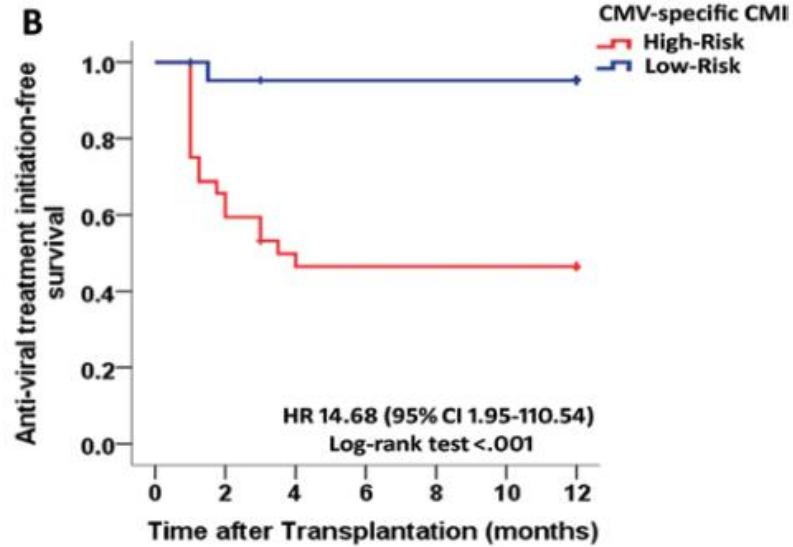
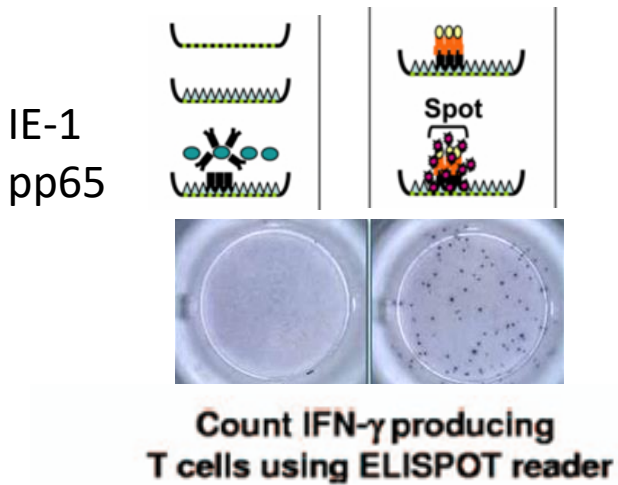
Lucia M et al. Transplant Int. 2015.

Context: CMV-Cell mediated immunity monitoring

RESPECT STUDY

R+, BSX induction, preemptive strategy, CMI d15

T-SPOT®.CMV



High-Risk (n)	32	19	14	14	14	14	14
Event-Free (n)	32	19	15	15	15	15	15
Low-Risk (n)	22	20	19	19	19	19	19
Event-Free (n)	22	21	21	21	21	21	21

Lucia M et al. Transplant Int. 2015.

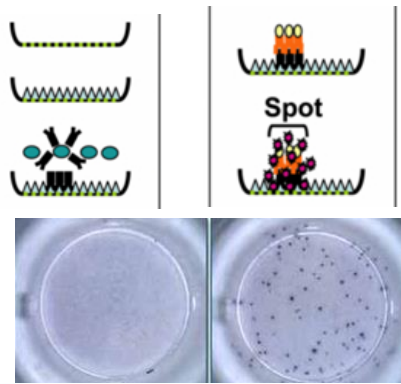
Jarque M et al., CID 2020

Context: CMV-Cell mediated immunity monitoring

RESPECT STUDY

T-SPOT®.CMV

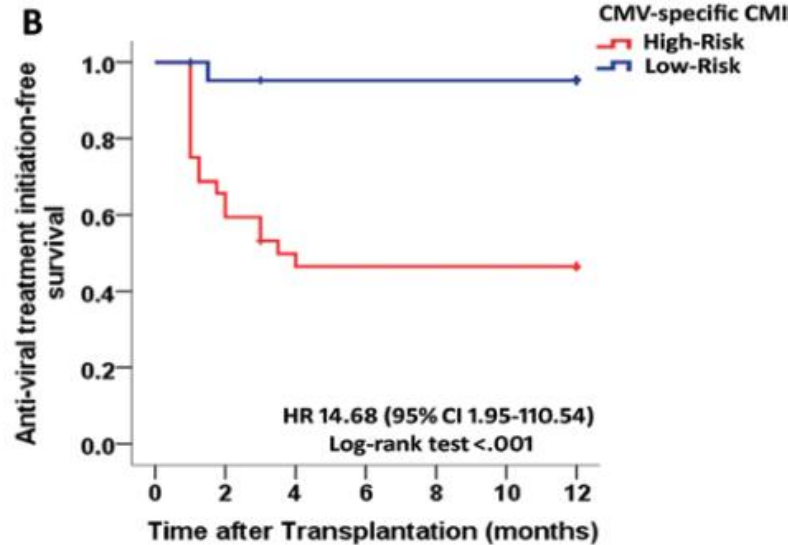
IE-1
pp65



Count IFN-γ producing T cells using ELISPOT reader

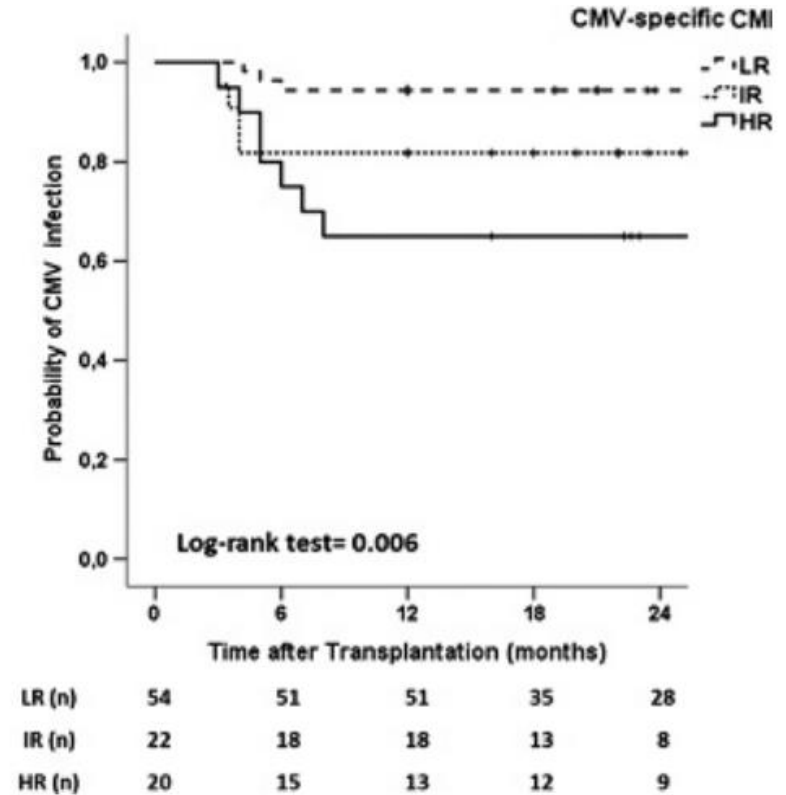
Lucia M et al. *Transplant Int.* 2015.

R+, BSX induction, preemptive strategy, CMI d15



Jarque M et al., *CID* 2020

R+, All inductions, prophylaxis strategy, CMI M3



Jarque M et al., *Transplantation* 2018

HYPOTHESIS AND OBJECTIVES

CMV-CMI can help the clinician to adapt CMV prevention in SOT recipients

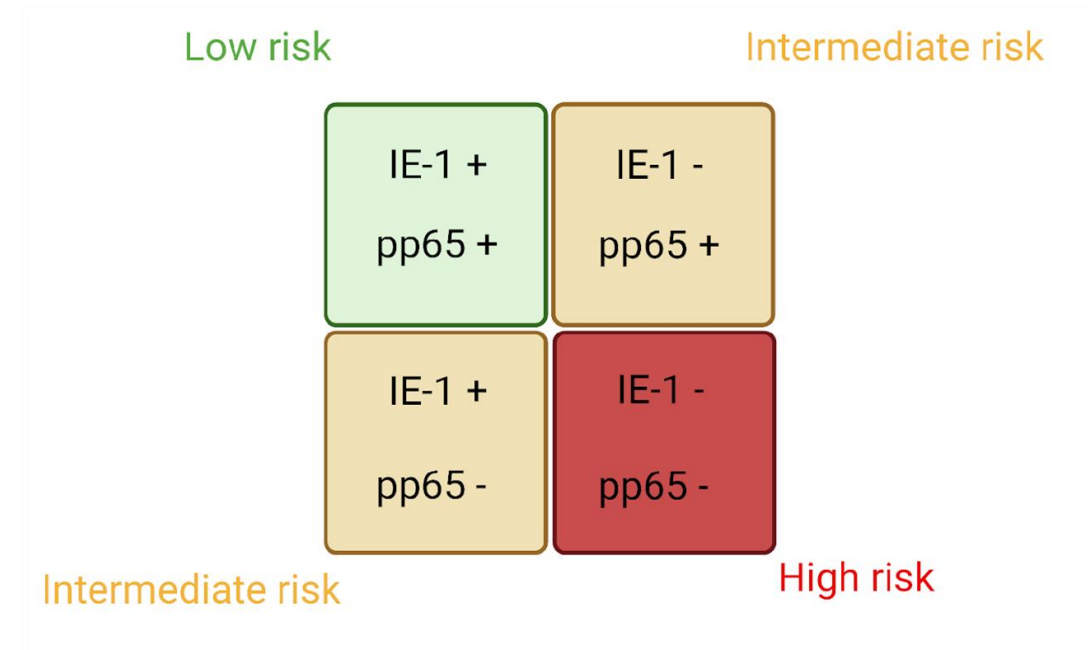
OBJECTIVE:

Assess the usefulness of CMV-CMI guided CMV prevention in real life

METHODS

Possibility to assess CMV-CMI offered to clinicians

Thresholds spots/250 000 cells	Guiding pre-emptive strategy	Guiding prophylaxis withdrawal
IE-1	40	40
pp65	170	135



A Guiding pre-emptive strategy

R+ BSX induction CMI day 10-15

- LR CMI ☐ 3-mo Preemptive (CMV PCR)
- HR/IR CMI ☐ 1 mo Prophylaxis or intensive 3-mo Preemptive
- CMV therapy if symptoms or >4000 DNA copies plasma

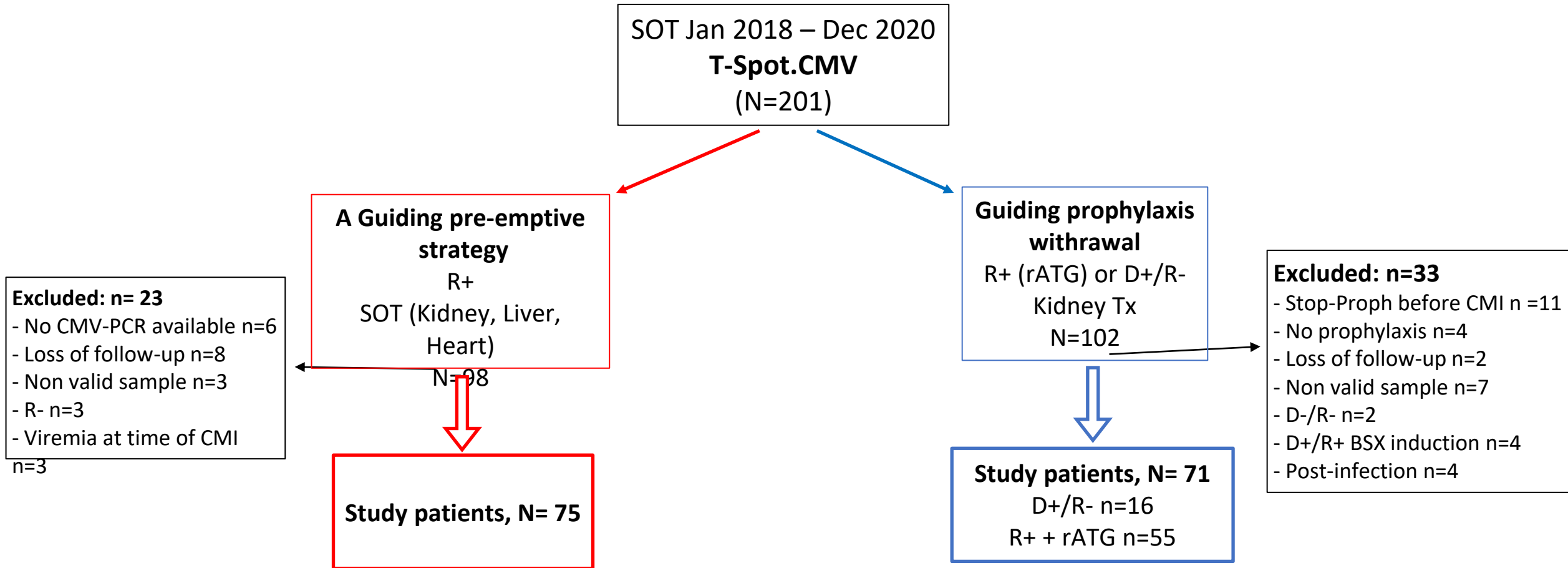
B Guiding prophylaxis withdrawal

R+ ATG induction and D+/R- with CMV prophylaxis CMI after 1.5 months

- LR CMI ☐ Stop Prophylaxis and secondary 3-mo Preemptive
- HR/IR CMI ☐ 1-mo Prophylaxis or intensive 3-mo Preemptive
- CMV therapy if symptoms or >4000 DNA copies plasma

Outcome : occurrence of CMV infection (symptomatic or high replication requiring treatment)

STUDY POPULATION



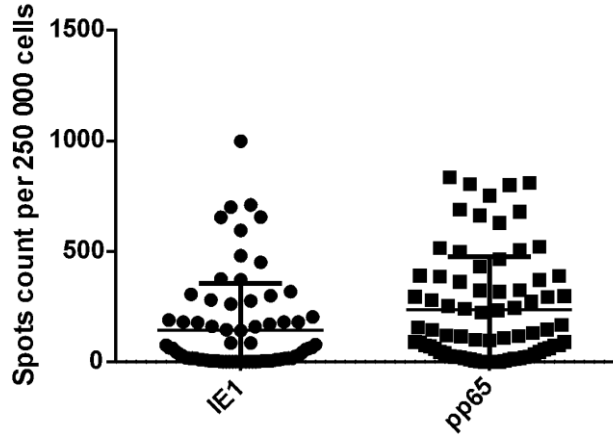
A. Guiding pre-emptive strategy

		Preemptive cohort n= 75
Recipient gender (male, n (%))		54 (72 %)
Recipient age (mean + SD)		56 +/- 9
Transplanted organ (n (%))		
	Liver	40 (53.3 %)
	Heart	25 (33.3 %)
	Kidney	10 (13.3 %)
Transplant rank (n (%))		
	1	71 (94.7 %)
	2	4 (5.3 %)
Induction treatment (n (%))		
	rATG	0
	Basiliximab	71 (94.7 %)
	None	4 (5.3 %)
Maintenance IS (n (%))		
	TAC + MMF	74 (98.7 %)
	TAC	1 (1.3 %)
Recipient CMV serology (n (%))		
	Positive	75 (100 %)
	Negative	0 (0 %)
Donor CMV serology (n (%))		
	Negative	12 (16 %)
	Positive	63 (84 %)
Time between Tx and CMI (days, mean + SD (range))		14.1 +/- 7.8 (6-40)

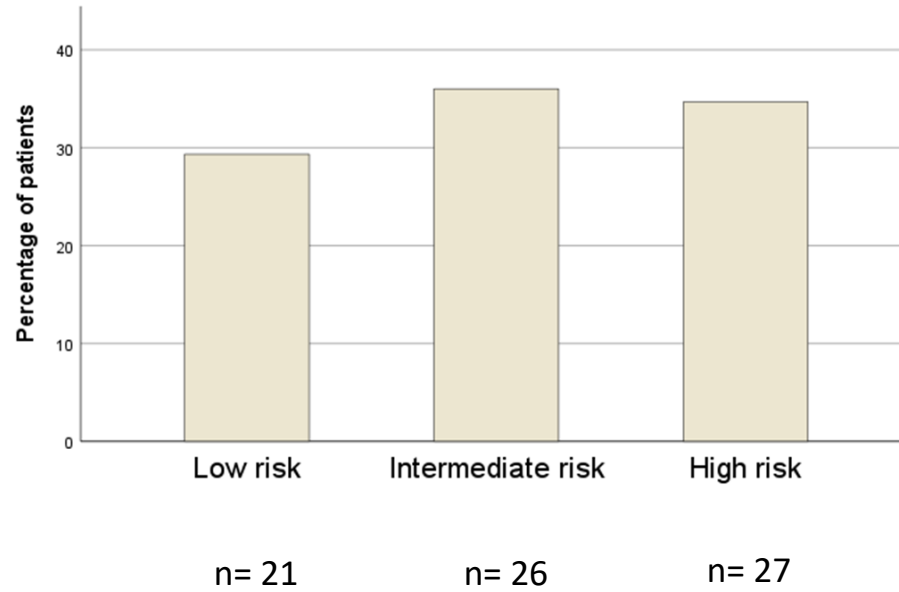
A. Guiding pre-emptive strategy

CMI results

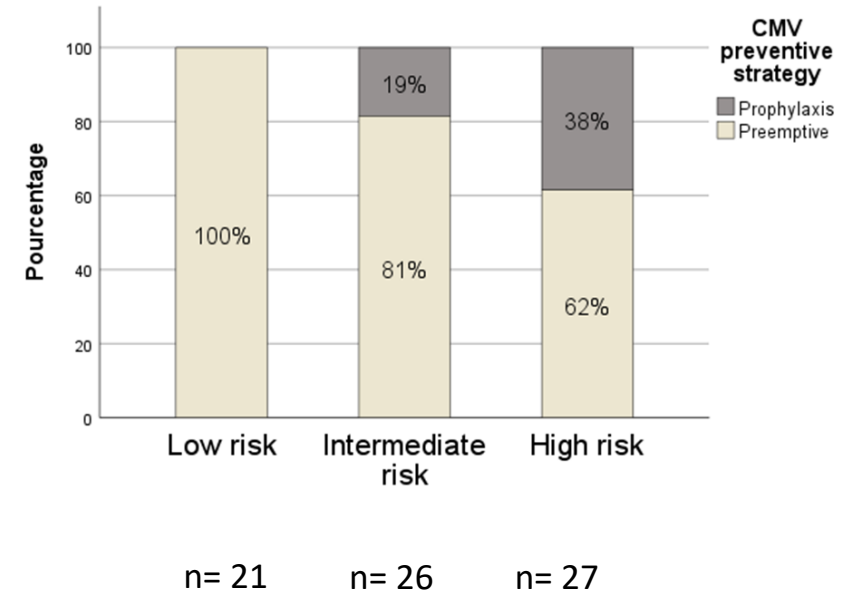
CMI raw results



CMI risk categories



CMV preventive strategy

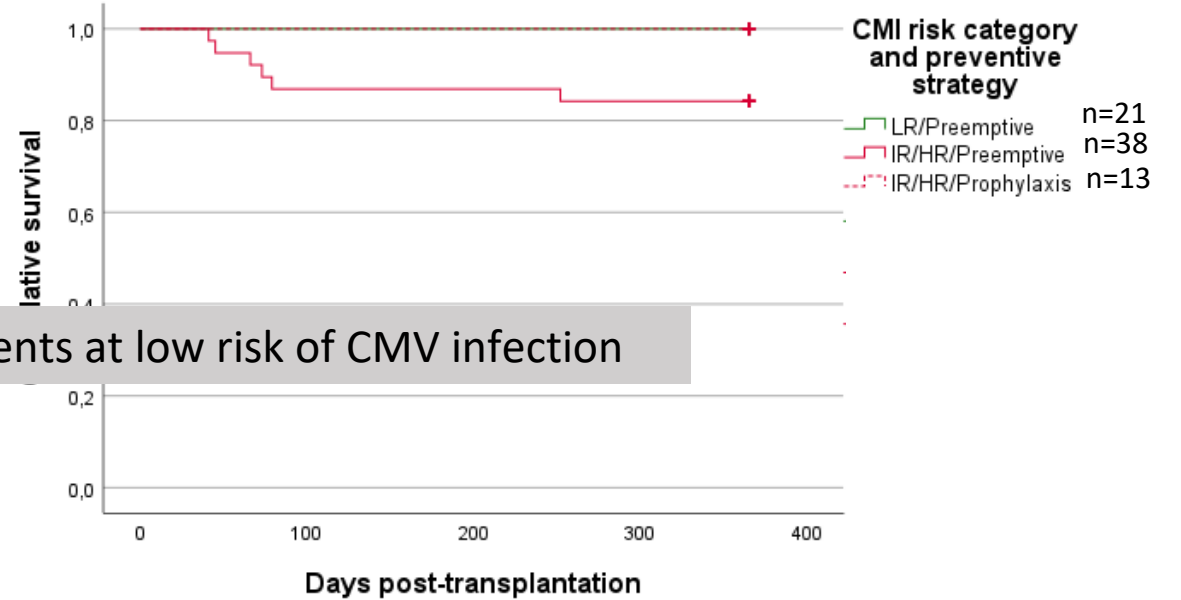
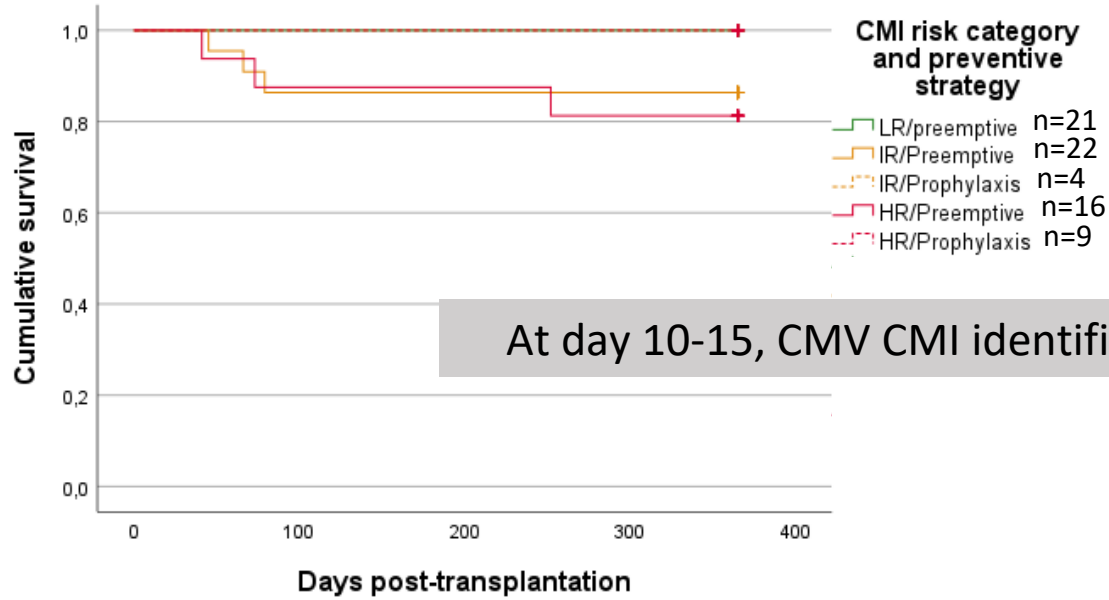


CMV prophylaxis started in 15 patients for a mean of 105.6 +/- 36.5 days

R+ BSX induction
CMI at day 10-15

A. Guiding pre-emptive strategy

CMV infection



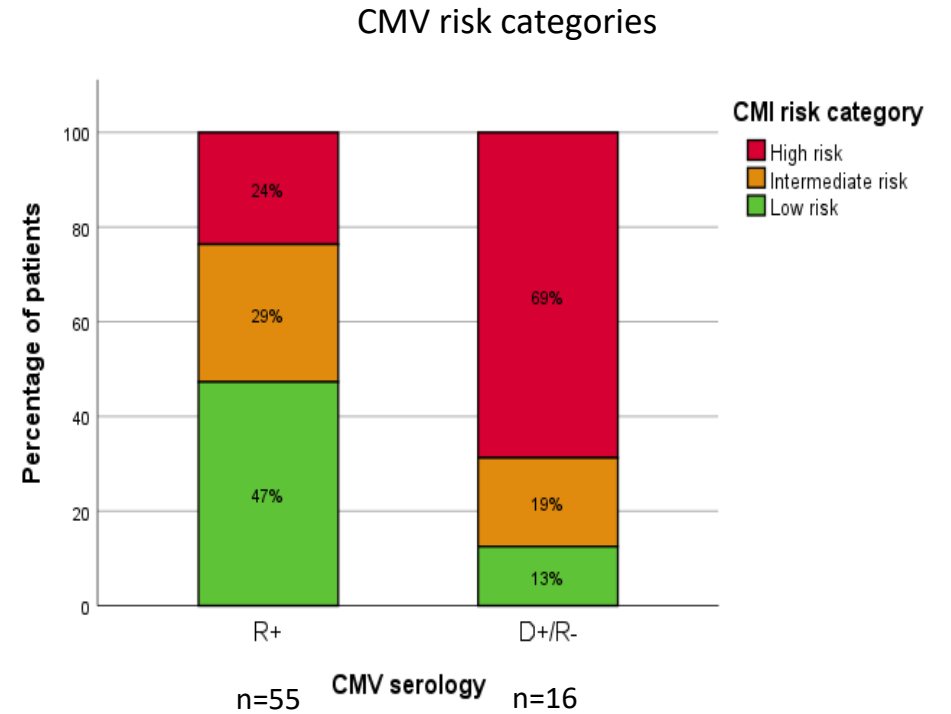
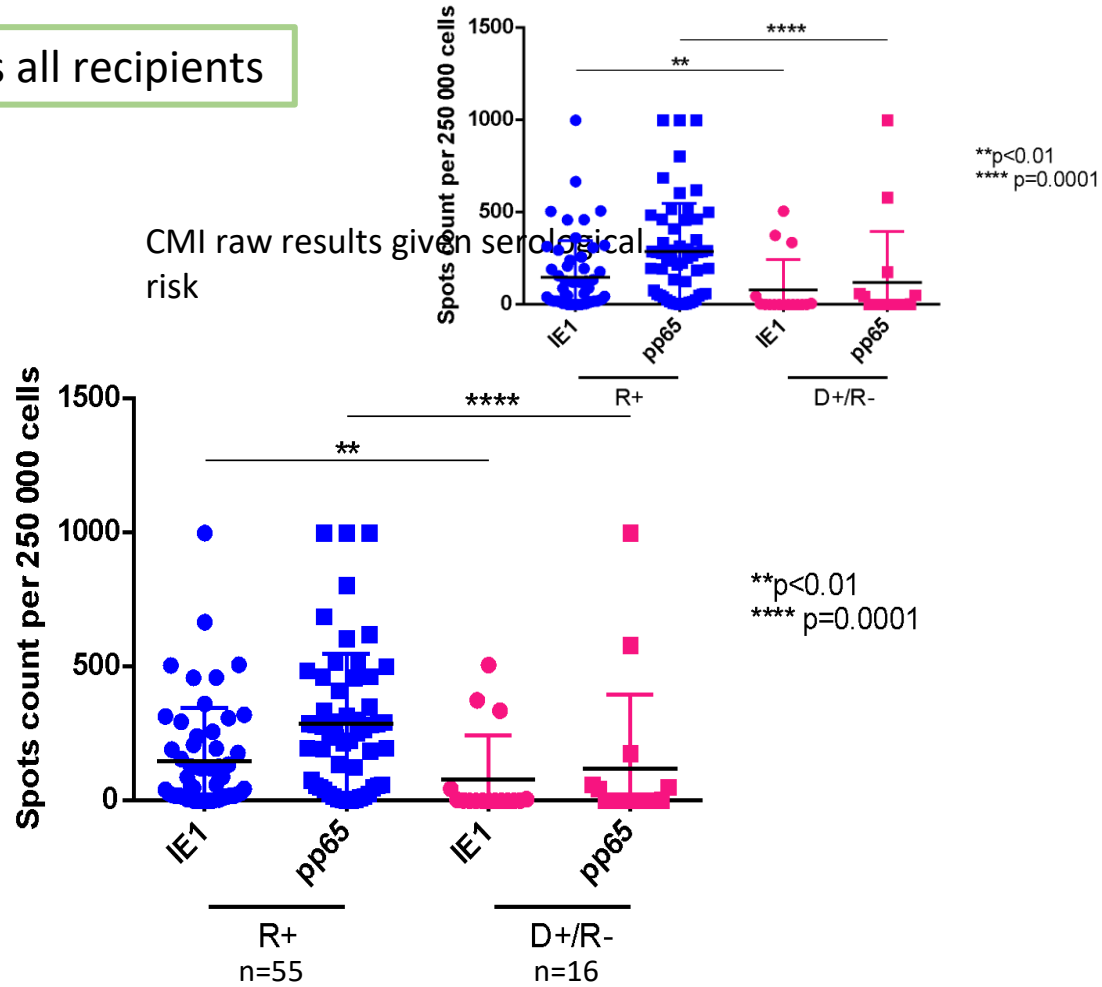
Mean time to event 92.7 +/- 72.6 days

B. Guiding prophylaxis withdrawal

	STOP PF cohort (n=71)	R+ (n=55)	D+/R- (n=16)
Recipient gender (male, n (%))	34 (48 %)	22 (31 %)	12 (75.0 %)
Recipient age (mean + SD)	55 +/- 13	57 +/- 12	50 +/- 13
Transplant rank (n (%))			
1	47 (66.2 %)	33 (60.0 %)	14 (87.5 %)
2	17 (23.9 %)	15 (27.3 %)	2 (12.5 %)
3	6 (8.5 %)	6 (10.9 %)	
4	1 (1.4 %)	1 (1.8 %)	
Induction treatment (n (%))			
rATG	57 (80.3 %)	54 (98.2 %)	3 (18.8 %)
Basiliximab	14 (19.7 %)	1 (1.8 %)*	13 (81.2 %)
Maintenance IS (n (%))			
TAC + MMF	69 (97.2 %)	54 (98.2 %)	15 (93.8 %)
TAC	1 (1.4 %)	1 (1.8 %)	
TAC + mTORi	1 (1.4 %)		1 (6.2 %)
Recipient CMV serology (n (%))			
Positive	55 (77.5 %)	55 (100 %)	0 (0 %)
Negative	16 (22.5 %)	0 (0 %)	16 (100 %)
Donor CMV serology (n (%))			
Negative	9 (12.7 %)	9 (16.4 %)	0 (0 %)
Positive	62 (87.3 %)	46 (83.6 %)	16 (100 %)
Time between Tx and CMI (days, mean + SD (range))	116 +/- 42,3 (47-255)	105.4 +/- 36.4 (47-255)	153.9 +/- 39.7 (86-212)

B. Guiding prophylaxis withdrawal

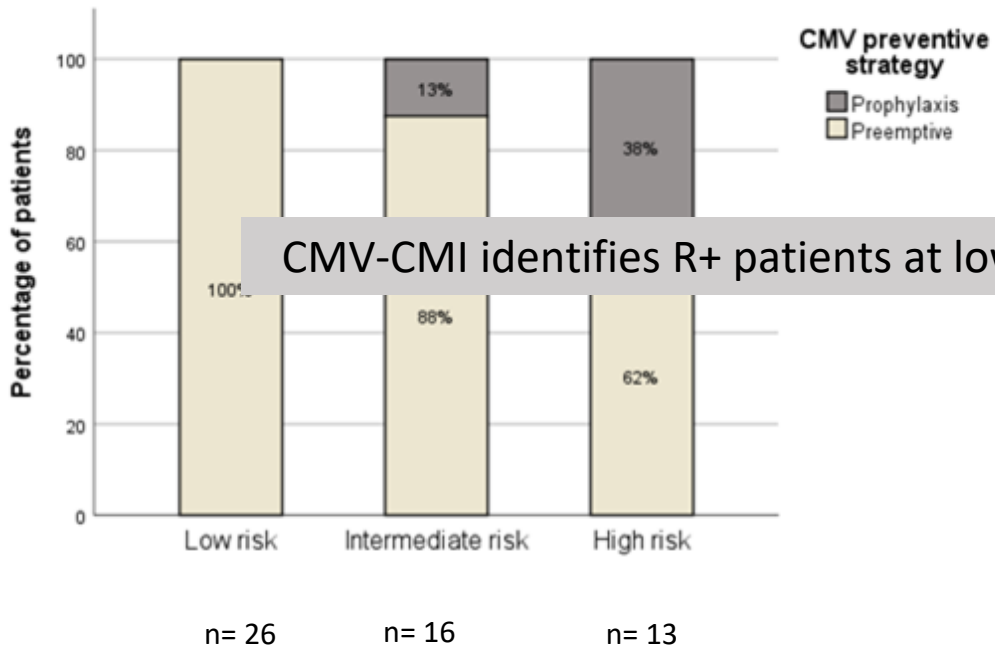
CMI results all recipients



B. Guiding prophylaxis withdrawal

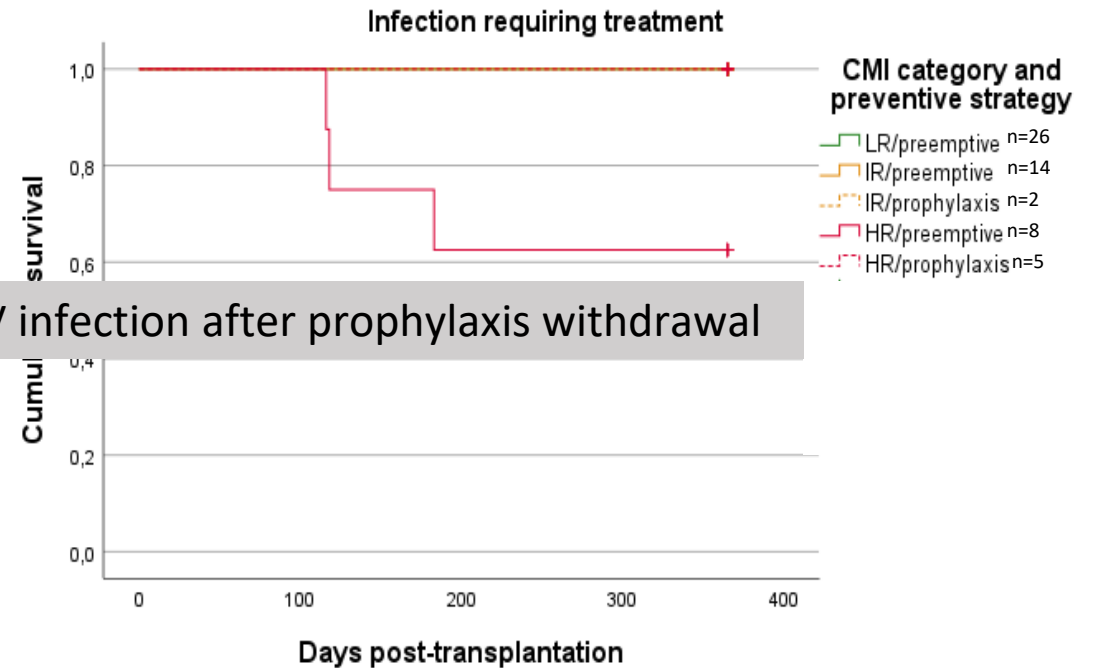
CMI results R+ n=55

CMV preventive strategy



CMV-CMI identifies R+ patients at low risk of CMV infection after prophylaxis withdrawal

CMV events R+



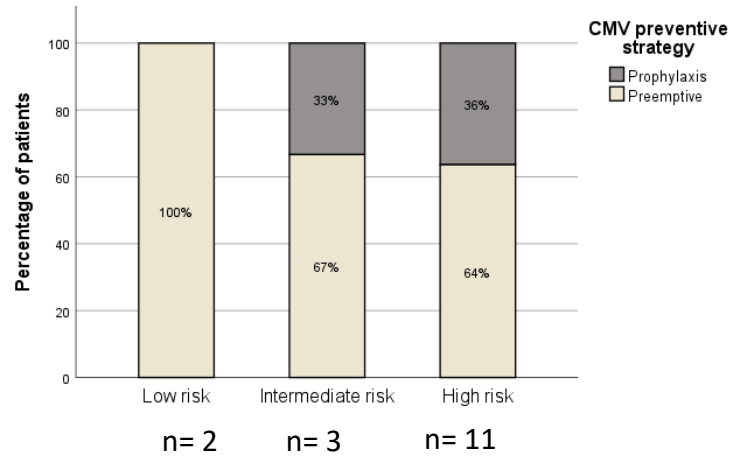
Log-rank test p<0.001

Mean prophylaxis duration 111.7 +/- 41.5 days

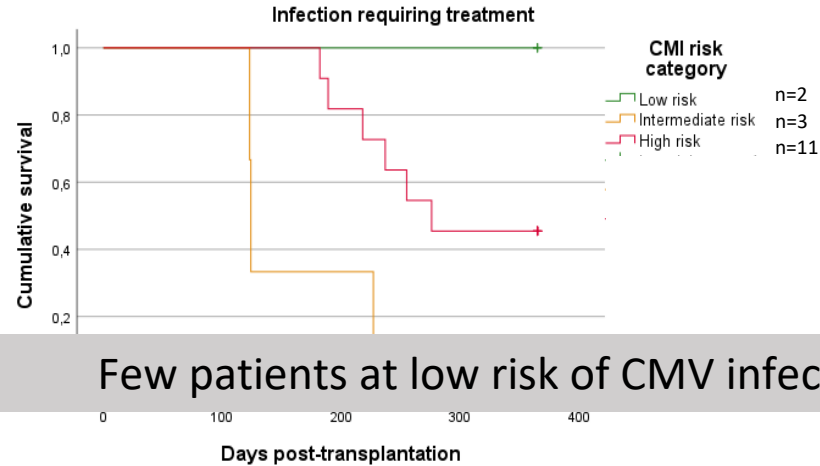
Mean time to event 139.0 +/- 31.1 days

CMI results D+/R- n=16

B. Guiding prophylaxis withdrawal

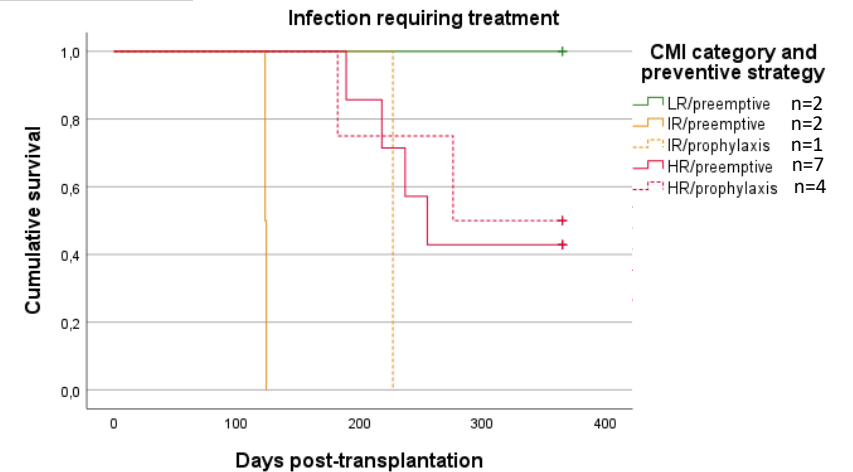


CMV events D+/R-



Few patients at low risk of CMV infection

Log-rank test p=0.004

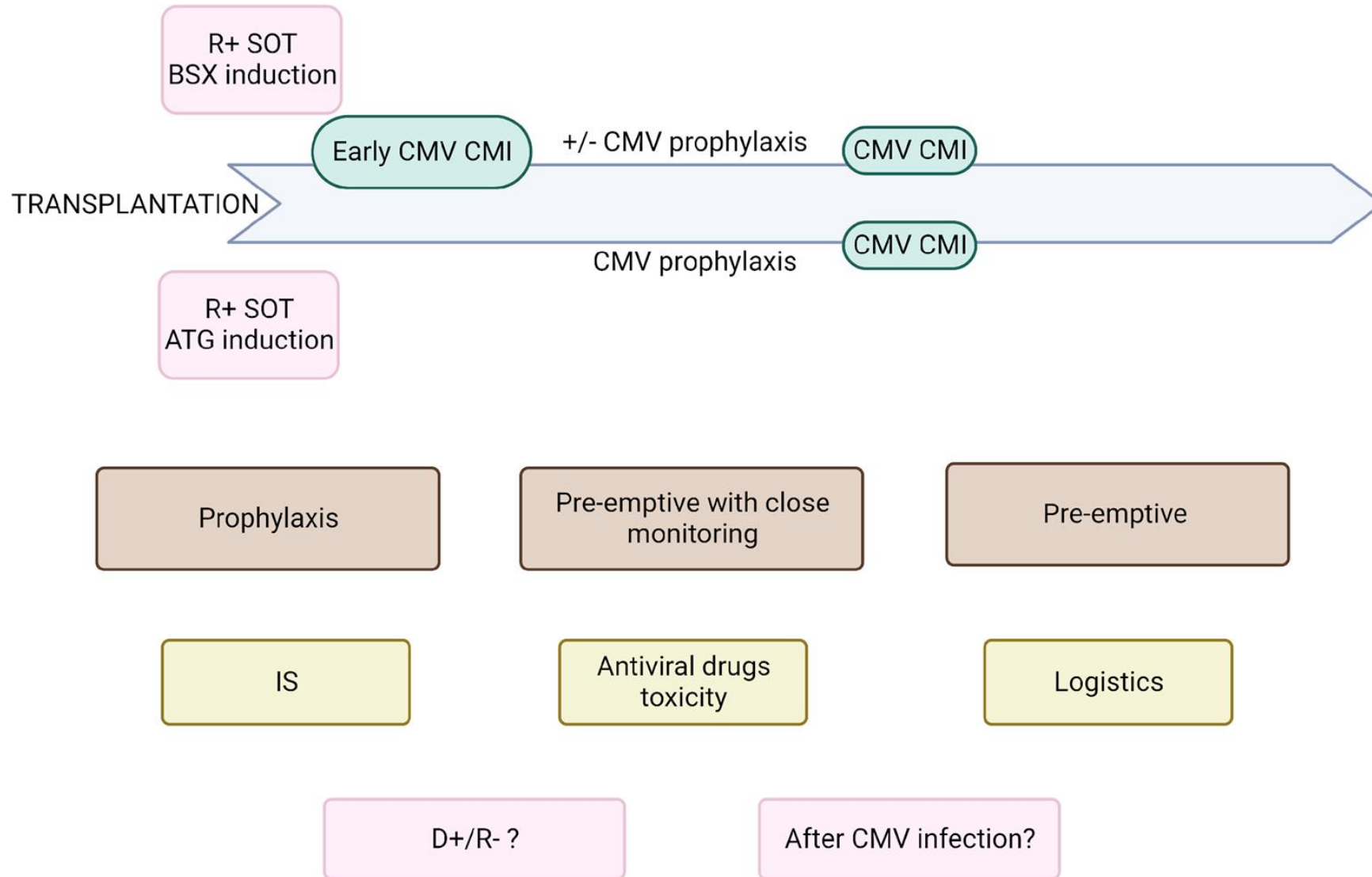


Log-rank test p<0.001

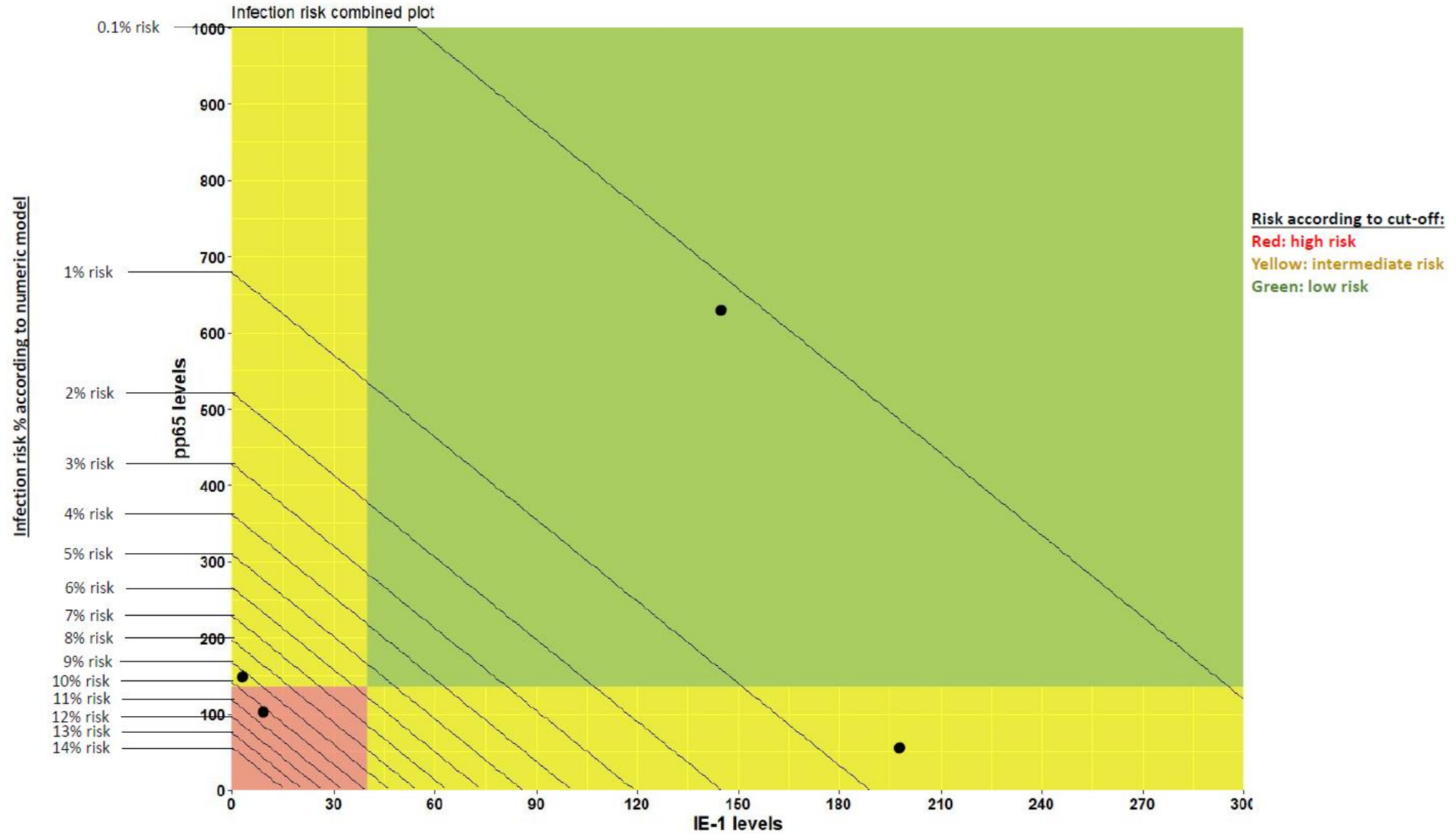
Mean prophylaxis duration 183.3 +/- 62.4 days

Mean time to event 203.4 +/- 50.8 days

SUMMARY AND PERSPECTIVES



SUMMARY and perspectives



ACKNOWLEDGEMENTS

Vall d'Hebron Research Institute:

- Elena Crespo
- Laura Donadeu
- Alba Torija
- Franc Casanova
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- Cristina Font

Bellvitge University Hospital:

- Edoardo Melilli
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- Jose Gonzalez-Costello
- Carles Diez
- Nuria Montero
- Alba Cachero
- Elena Garcia

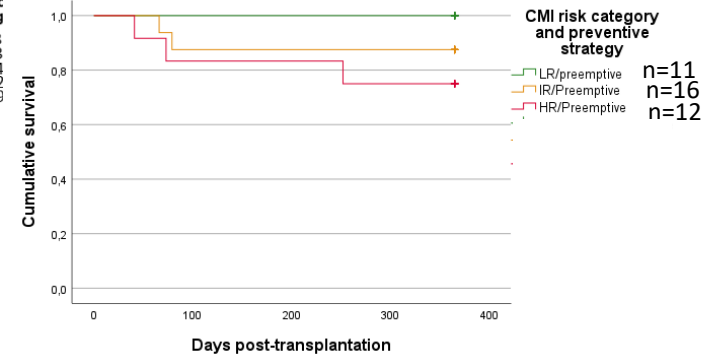
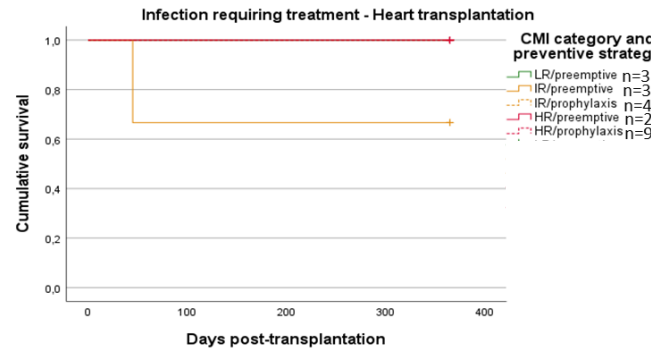
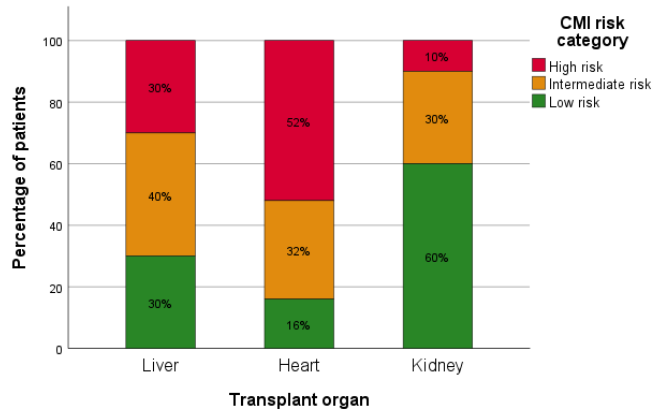
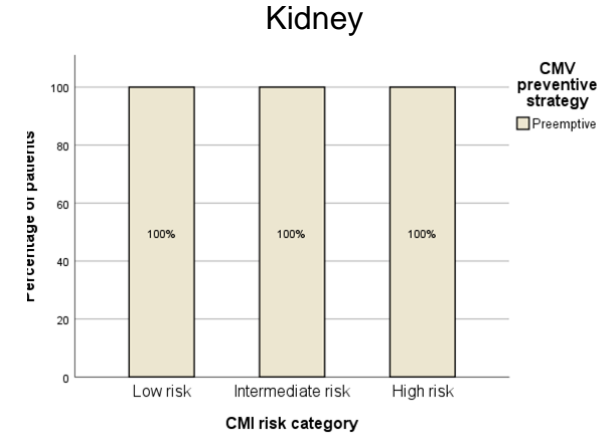
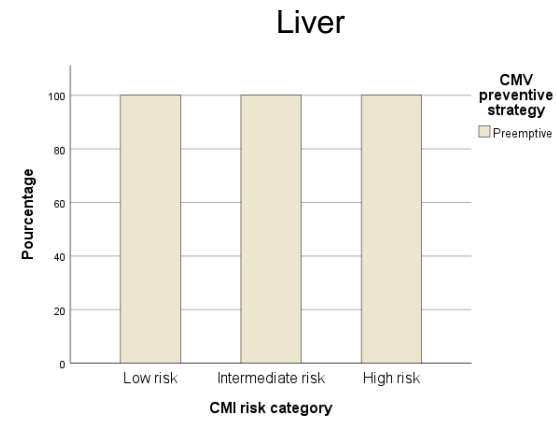
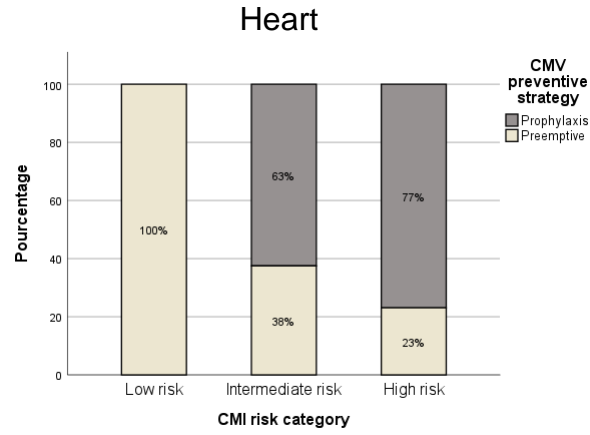
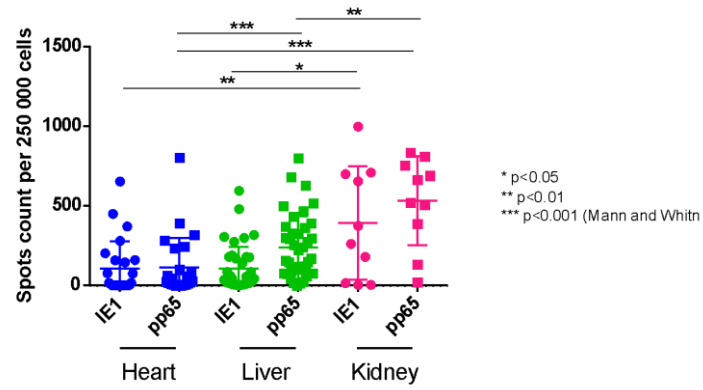
Vall d'Hebron University Hospital:

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- Ignacio Cidraque



CMI results by organ

A. Guiding pre-emptive strategy

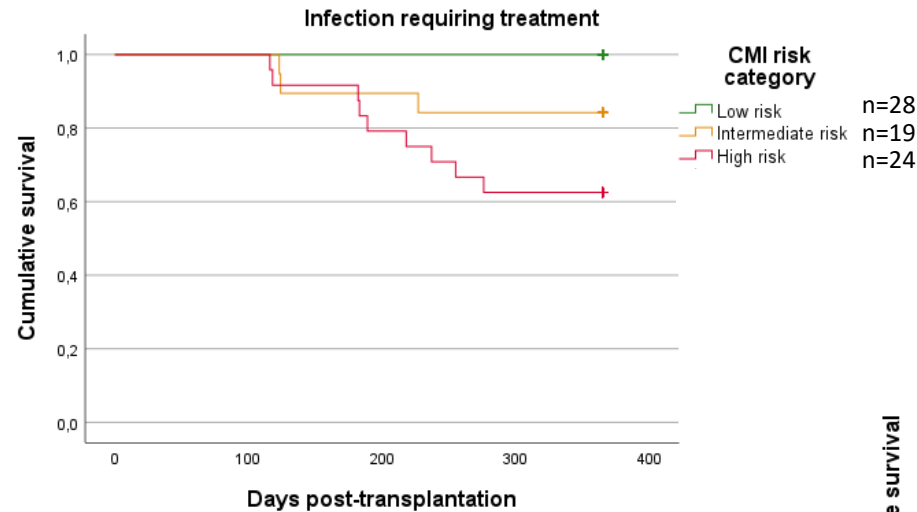
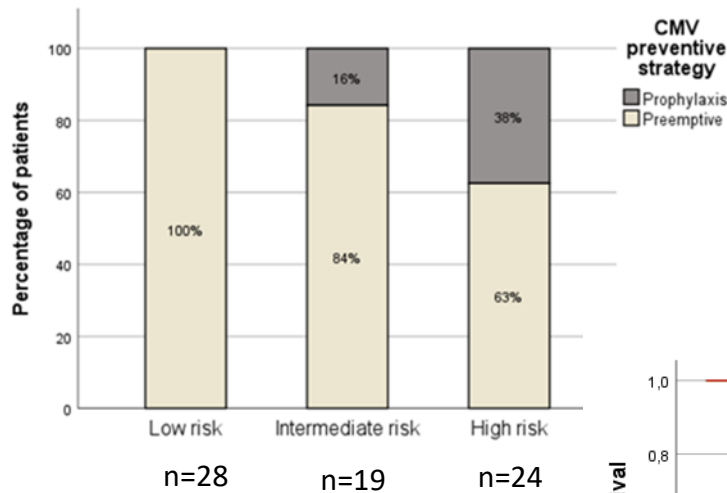


Kidney no infection requiring treatment

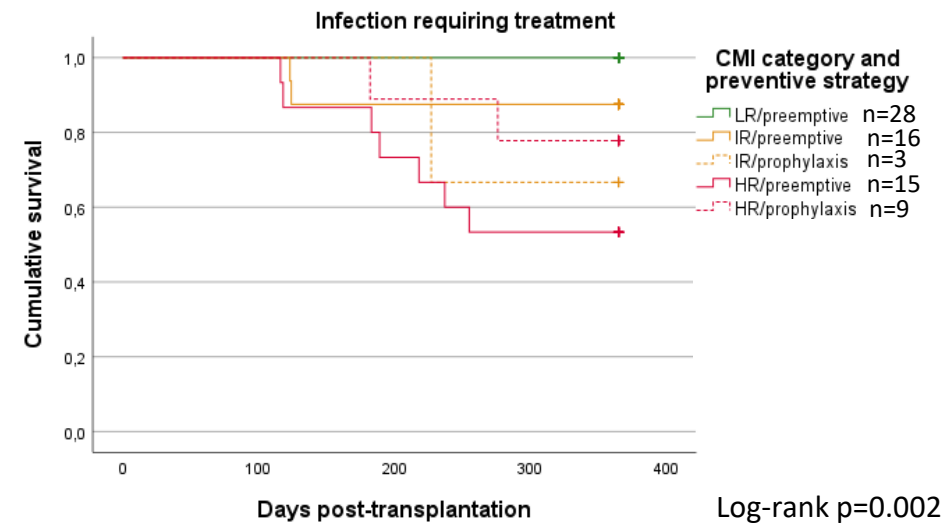
10 patients have had a CMI before stop PF : LR 1 IR 3 HR 6

B. Guiding prophylaxis withdrawal

CMV events all recipients



Log-rank p=0.002



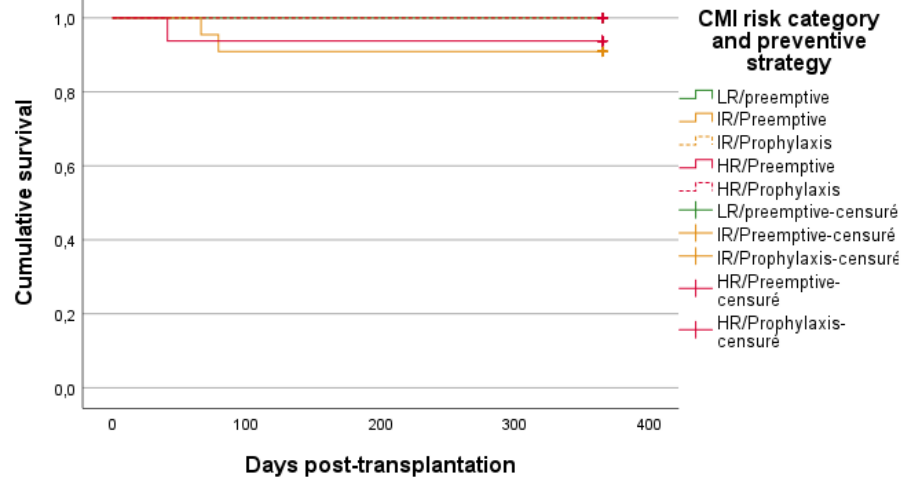
Log-rank p=0.002

Mean prophylaxis duration 127.8 +/- 55.7 days

Mean time to event 187.3 +/- 54.4 days

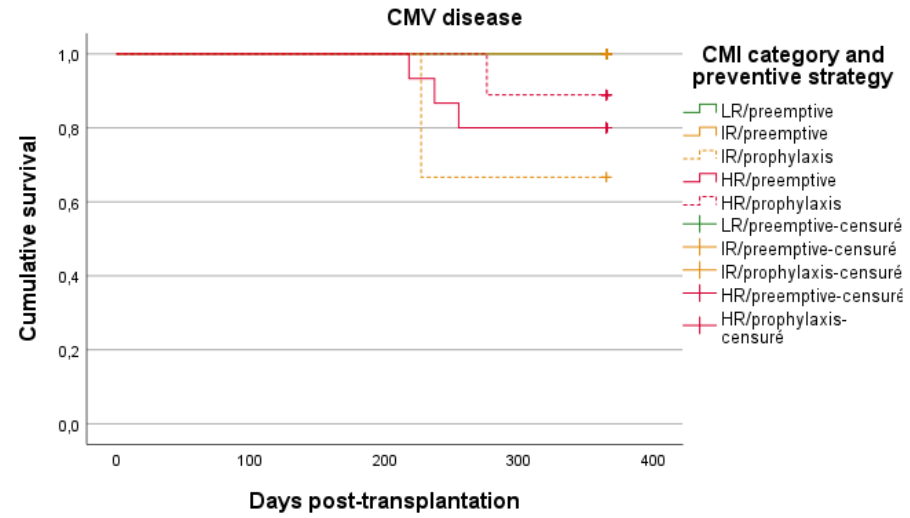
CMV disease

Preemptive



P=0.531

Stop PF D+/R-

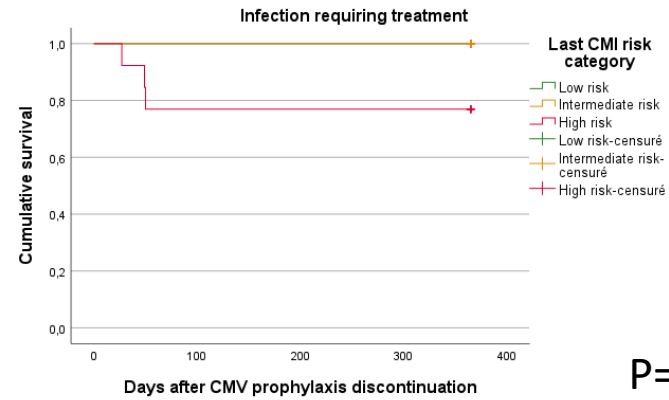
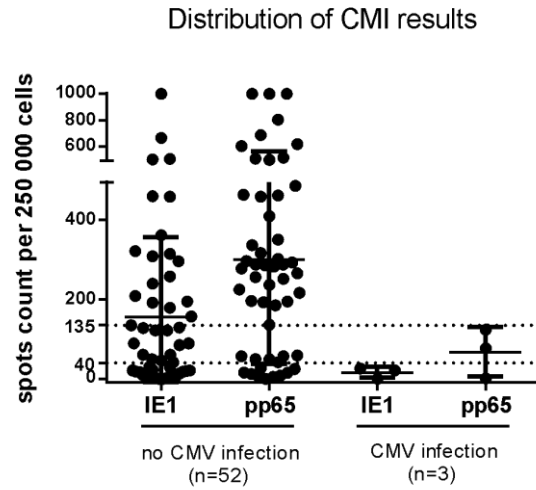


P=0.022

Stop PF R+ No disease

STOP PROPHYLAXIS STRATEGY R+

Last ELISPOT before STOP PF (but all events in the group preemptive)



P=0.005

No disease event