Evaluation of novel programme aimed at reducing the risk of severe viral infections, including cytomegalovirus, following solid organ transplantation

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BACKGROUND
CMV infection frequently complicates the course after solid organ transplantation and may cause life threatening disease if not diagnosed early

• Since many solid organ transplant recipients at our hospital presented with severe CMV infection, we developed The MATCH Programme

AIM
• Evaluate patients transplanted in the first year (and with ≥ 6 months follow-up) after introducing the MATCH program and compare their CMV infection outcome with that of patients transplanted in two previous calendar periods

OVERVIEW OF THE MATCH PROGRAMME
Main purpose is to standardize several key procedures in question required for diagnosis and treat viral infections early after they emerge. The principles of the MATCH programme are shown in Figure 1. Several stakeholders are involved:

Transplant coordinators
• Perform the registration of donor and recipient in the database
• At the time of the transplantation, blood from both donor and recipient is analysed using a standardized protocol

Clinical laboratories
• Deliver real-time electronic interface to their databases ensuring direct access to all completed viral analyses

Clinical department
• Advises CMV chemo prophylaxis (primary intervention) and treatment (secondary interventions) according to the MATCH programme
• Ensures schema’s for screening for viral infection are followed

MATCH database (central coordination)
• Based on algorithms for matching donor and recipient viral status at time of transplantation recommend CMV chemo prophylactic and monitoring schema for emerging viral infections according to individual a priori risk
• This information is electronically communicated to the clinical department
• When a viral analysis shows an abnormal value or is missing, an electronic alarm is generated and appropriate action is taken

• Via these alarms + continuous assessment of viral analyses and clinical status, monitoring schema and medical interventions are modified.
• Updated patient plans are electronically communicated to the clinical department
• A steering committee with representatives from all stakeholders make strategic and scientific decisions according to the programme

METHODS
Patients and study design
• All patients transplanted from 2007 to 2011 were included in the analysis
• Recipients transplanted after implementation of the program (2011) were compared to that of recipients transplanted prior to (2007-2008) and while (2009-2010) the program was developed
• During the first year after transplantation the incidence of CMV infection (two consecutive CMV PCR > 300 copies/mL) among recipients transplanted in each of the three calendar periods was determined
• The severity of the infection (mild ≤ 5,000 / moderate 5,000-29,999 / severe ≥ 30,000 copies/mL) at the time of diagnosis was assessed
• Rate of admission related to CMV infection was also determined

Statistical methods
• Risk factors for moderate to severe CMV infection and hospital admission were explored using unadjusted and adjusted Cox and logistic regression models. Models were adjusted for age, gender and all variables shown

RESULTS
Tables and figures
• Characteristics of 809 included patients at the time of the transplantation are depicted in Table 1
• A total of 448 (55%) developed CMV infection and the incidence did not vary over calendar time (p=0.3, Figure 2)
• At the time of diagnosis of CMV the prevalence of moderate to severe infection decreased from 49% to 44% and to 13% over calendar time, Figure 3
• Factors associated with moderate to severe CMV infection at the time of diagnosis were calendar time (adjusted hazard ratio (HR) 2011 versus 2007-2008 = 0.68 (0.92 to 0.3) [99% CI]) and Donor/Recipient CMV IgG matching HR (D+/R-/D-/R+) = 7.6 (1.1 to 14.2) [99% CI]), Figure 4
• The rate of admission due to CMV decreased from 44% to 55% to 17% over calendar time, Figure 3
• Factors associated with admission were calendar time (adjusted odds ratio (OR) 2011 versus 2007-2008 = 0.16 (0.10-0.25) [99% CI]) and Donor/Recipient CMV IgG matching OR (D+/R-/D-/R+) = 2.6 (1.2 to 5.8) [99% CI]), Figure 5

CONCLUSION
• By use of systematic risk stratification, aimed at screening for emerging infections at times when risk is high, the clinical prognosis of CMV infection radically improved
• This novel program can be implemented at any transplant unit