Ability of cytomegalovirus immune monitoring assays to predict CMV related outcomes in transplant patients: a systematic review

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Berkeley Public Health

Methods

- Complete search strategy elaborated by John Reynolds, librarian at the University of Miami
- 3 components:

18	Monitoring, Immunologic/	1,523
19	((immun* adj3 (monitor* or surveill*)) or immunosurveil*).ti,ab,kf.	18,653
20	((CMV or CMVi) adj3 (monitor* or surveill*)).ti,ab,kf.	667
21	Immunity, Cellular/	53,439
22	((cell or cellular or lymphocyt* or adoptive) adj3 (immunit* or immunol* or immune-response* or defense)).ti,ab,kf.	75,722

Methods

Inclusion

Patient population
- HSCT - both allo and auto
- SOT - all types
- >10 patients or at least 10 patients that meet the study criteria

Tests
- ELISPOT and derivatives (T-SPOT, Elisa)
- Quantiferon and derivatives
- intracellular cytokine staining with flow cytometry
- Other tests such as “homemade” tests.

Patient outcomes included:
- Change in treatment management
- CMV infection
- viral load positivity (just viremia is ok)
- Antigenemia
- Reactivation
- Clinical symptoms of CMV

Study type
- Observational studies
- Interventional studies
- Stored specimen studies
- Poster/conference abstract with sufficient data

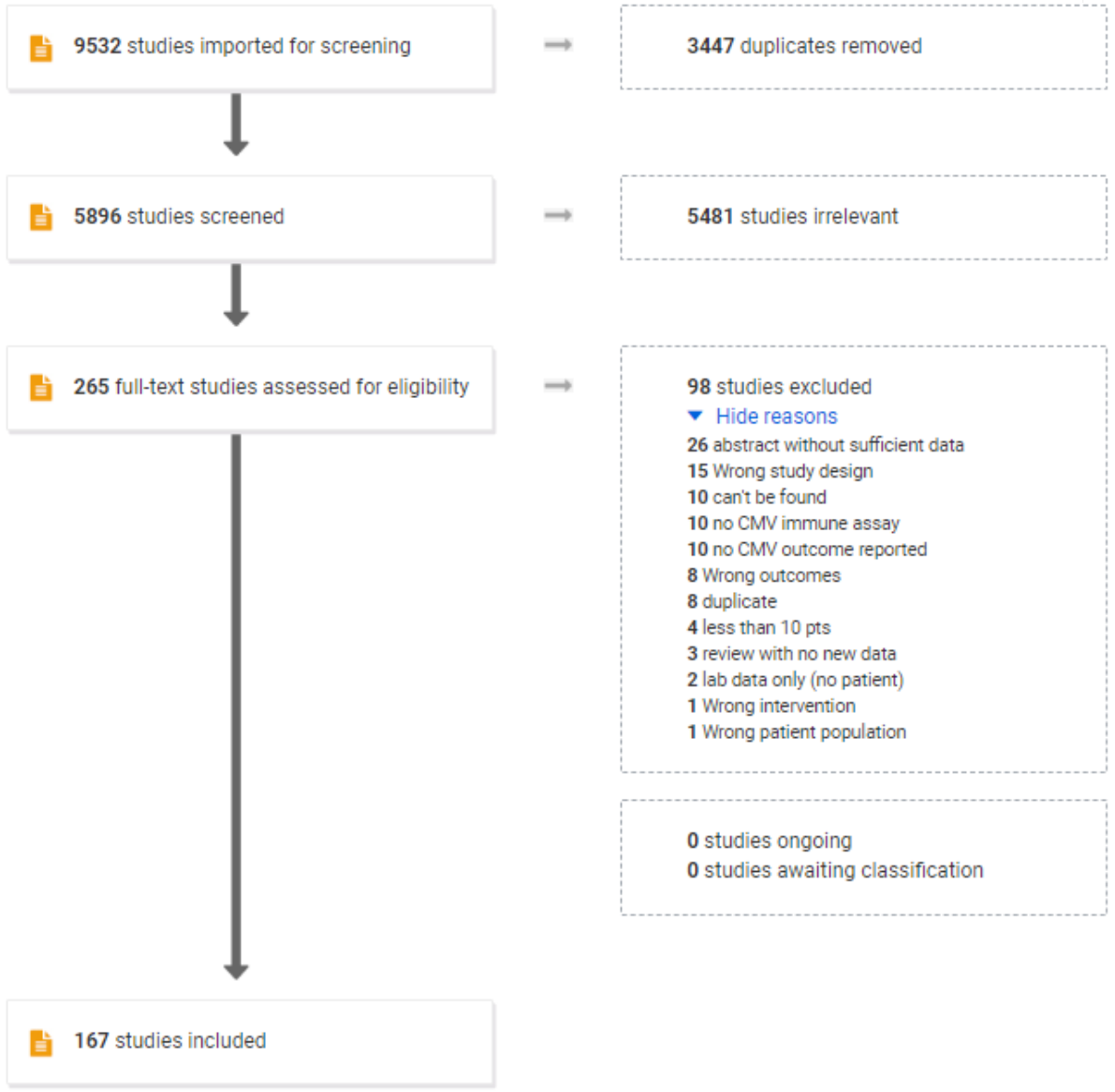
Exclusion

Patient population
- not HSCT and/or
- not SOT
- <10 patients

Tests
- No quantitative CMV immune assay reported
- Cytokine profiles studies without quantification

Patient Outcomes
- No CMV related outcome reported

Types of studies:
- Poster/conference abstract with insufficient data
- Review without new data
- Laboratory based studies without patient information
- Natural history studies
- Animal Studies
- duplicates


9532 studies imported for screening
3447 duplicates removed
5896 studies screened
5481 studies irrelevant
265 full-text studies assessed for eligibility
98 studies excluded
Hide reasons
26 abstract without sufficient data
15 Wrong study design
10 can't be found
10 no CMV immune assay
10 no CMV outcome reported
8 Wrong outcomes
8 duplicate
4 less than 10 pts
3 review with no new data
2 lab data only (no patient)
1 Wrong intervention
1 Wrong patient population
0 studies ongoing
0 studies awaiting classification
167 studies included

Extraction

Article DOI	Author	year	title	sample size	type of transplant	patient gender	patient age	Serostatus	patient outcome recorded
https://doi.org/10.1128/JCM.06406-11	Davide Abate, Marta Fiscon, Alda Saldan, Simona Cofano, Carlo Mengoli, Dino Sgarabotto, Chiara d'Agostino , Luisa Barzon, Riccardo Cusinato, Giuseppe Toscano, Giuseppe Feltrin, Antonio Gambino, Gino Gerosa, Giorgio Palù	2012	Human Cytomegalovirus-Specific T-Cell Immune Reconstitution in Preemptively Treated Heart Transplant Recipients Identifies Subjects at Critical Risk for Infection	58	48 heart transplants, 10 pre-transplant	female: 8, male: 40	median: 59 (11-74)	R+D+ and R+D-	CMV infection is defined as detection of viremia at >1,000 copies/ml of whole blood. CMV disease was defined as symptomatic clinical manifestations with fever and malaise associated with detectable CMV viremia and not ascribable to any other infection or condition

type of assay	assay threshold studied	PPV,NPV, sensitivity, specificity	antigen studied	timing	assay results vs patient outcome	conditioning regimen	antiviral treatment
ELISPOT	50 and 100 spots	NA	pp65	Twenty-nine patients were analyzed both before and after 100 days posttransplant, while 19 patients were analyzed once for collection of a single data point before or after 100 days posttransplant	Patients protected from CMV viremia displayed statistically significantly higher ELISPOT levels (median, 173 spots; range, 0 to 1,000 spots) than HTXs with the occurrence of viremia (median, 18 spots; range, 1 to 267 spots). On the basis of the ELISPOT levels, we arbitrarily grouped HTXs into high responders (>100 spots), midresponders (>50 to <100 spots), and low responders (<50 spots) ($p<0.05$)	antithymocyte treatment (recombinant antithymocyte globulin, 20 mg/kg of body weight/day) for 4 days posttransplant	Transplant patients were treated according to a preemptive strategy, defined as described previously (21, 29, 35, 37) and consisting of the initiation of antiviral treatment upon the detection of a viral load (CMV DNAemia) above 5,000 copies/ml. Anti-CMV preemptive treatment included oral administration of valganciclovir (Valcyte; Roche) at a standard dose (900 mg twice a day) or intravenous ganciclovir (5 mg twice a day) corrected according to renal function.