from the CHS[2] for parental stress measures. L.A.FANS did not use validated stress measures; therefore, we chose psychosocial stressors that pertain to the adolescent's physical surroundings or family functioning that have previously been associated either with a stress response or with reduced lung function (for detailed discussion of selected stressors, see the Discussion section in this article's Online Repository at www.jacionline.org). Psychosocial stressors, which often cluster in economically deprived neighborhoods, may explain some of the adverse effects on respiratory health observed with measures of socioeconomic status.[5] The biologic underpinnings for synergisms between air pollution and stress on lung function may be found in the immune response and inflammatory reactions.[6,7] Many air pollutants consist of free radicals, which in the lung tissue result in oxidative stress that generates an inflammatory response, releasing additional free radicals that ultimately damage lung tissue.[6] Psychosocial stressors, acting through the hypothalamic-pituitary-adrenal axis modifications, also heighten inflammatory activity and modulate immune function,[8] potentially increasing susceptibility to environmental insults. This pathway may contribute to some of the differential pulmonary vulnerability to air pollutants observed in those with higher levels of psychosocial stress.[2]

Briefly, strengths of our study include the use of adolescent self-reported psychosocial stressors. In addition, our spirometry estimates were sensitive to the effects of air pollution and both measures were similar to estimates obtained for air pollutants and pulmonary function from the CHS.[9] However, validated or more psychometrically sound instruments would have been preferential to the stress measures that we used. Although we chose psychosocial stressors based on empirical evidence of cortisol activity in other research, without such biomarkers, we do not know whether reported psychosocial stressors caused a stress response in the adolescent. Our findings of paternal absence are difficult to interpret, as the adolescents were not further queried about their own feelings about the familial composition or related stress. In addition, our sample size did not allow us to analyze pulmonary function as a change from predicted value from a standard population, nor was our sample size large enough to calculate our own standard reference. Thus, we have reported absolute changes in pulmonary function values.

Healthy growth and development of pulmonary function in childhood and adolescence is instrumental for respiratory health in adulthood. Our findings contribute modest evidence to the hypothesis that psychosocial stress modifies the effects of air pollutants on lung function, and we hope they may inspire researchers to measure stress when conducting research on respiratory health.

Gretchen Bandoli, PhD[a]
Ondine von Ehrenstein, PhD[b]
Jo Kay Ghosh, PhD[c]
Beate Ritz, MD, PhD[a]

From the Departments of [a]Epidemiology and [b]Community Health Sciences, Fielding School of Public Health, University of California, Los Angeles, Calif; [c]Independent Researcher, Los Angeles, Calif. E-mail: gbandoli@ucla.edu.

The collection of spirometry and air pollution data was funded by the California Air Resources Board (04-323). The National Institute of Environmental Health Sciences (NIEHS) provided additional funding for the analysis and manuscript preparation (grant no. R03ES025908-01). RAND Corporation collected all other data (RAND Center for Population Health and Health Disparities (NIEHS grant no. 1P50 ES012383). California Air Resources Board, RAND Corporation, and NIEHS had no involvement in the design, analysis, or preparation of this manuscript.

Disclosure of potential conflict of interest: The authors have received research support from the California Air Resources Board (04-323), RAND Center for Population Health and Health Disparities (National Institute of Environmental Health Sciences [NIEHS] grant no. 1P50 ESO12383), and the NIEHS (grant no. R03 ES025908-01).

REFERENCES

1. Chen Z, Salam MT, Eckel SP, Breton CV, Gilliland FD. Chronic effects of air pollution on respiratory health in Southern California children: findings from the Southern California Children's Health Study. J Thorac Dis 2015;7:46-58.
2. Islam T, Urman R, Gauderman WJ, Milam J, Lurmann F, Shankardass K, et al. Parental stress increases the detrimental effect of traffic exposure on children's lung function. Am J Respir Crit Care Med 2011;184:822-7.
3. Astell-Burt T, Maynard MJ, Lenguerrand E, Whitrow MJ, Molaodi OR, Harding S. Effect of air pollution and racism on ethnic differences in respiratory health among adolescents living in an urban environment. Health Place 2013;23:171-8.
4. Peterson CE, Pebley AR, Sastry N, Yuhas K, Ghosh-Dastidar B, Haas AC, et al. The Los Angeles Family and Neighborhood Survey, Wave 2 user's guide and codebook. 2011. Santa Monica, CA: RAND Corporation; 2012. Available at: http://www.rand.org/pubs/working_papers/WR240z20.html.
5. Clougherty JE, Kubzansky LD. A framework for examining social stress and susceptibility to air pollution in respiratory health. Environ Health Perspect 2009;117:1351-8.
6. Kelly FJ. Oxidative stress: its role in air pollution and adverse health effects. Occup Environ Med 2003;60:612-6.
7. Hänsel A, Hong S, Cámara RJA, von Känel R. Inflammation as a psychophysiological biomarker in chronic psychosocial stress. Neurosci Biobehav Rev 2010;35:115-21.
8. Wright RJ. Epidemiology of stress and asthma: from constricting communities and fragile families to epigenetics. Immunol Allergy Clin North Am 2011;31:19-39.
9. Peters J. Epidemiologic investigation to identify chronic effects of ambient air pollutants in Southern California. Prev Med (Baltim) 2004. Available at: http://www.arb.ca.gov/research/apr/past/94-331a.pdf. Accessed July 23, 2015.

Available online April 30, 2016.
http://dx.doi.org/10.1016/j.jaci.2016.04.012

Specific T cells for the treatment of cytomegalovirus and/or adenovirus in the context of hematopoietic stem cell transplantation

To the Editor:

Viral infections following allogeneic hematopoietic stem cell transplantation (HSCT) are associated with elevated morbidity and mortality rates because HSCT exposes patients to a transient state of profound T- and B-cell immunodeficiency. Most post-HSCT viral infections are caused by the endogenous reactivation of opportunistic pathogens such as adenovirus (ADV), cytomegalovirus (CMV), and EBV.[1] The risk of mortality associated with these viral infections is directly proportional to (1) the degree of HLA mismatch between the donor and the recipient and (2) the time of T-cell reconstitution. Hence, this risk is lower in patients with T-cell–repleted graft versus patients receiving T-cell–depleted transplant.[2] During the posttransplant period, several prophylactic or preemptive antiviral treatments may be partially effective by inhibiting viral replication and thus stabilizing the viral load.[3,4] However, antiviral drugs can also induce drug resistance and be responsible for organ toxicity.[5]

Because the transfer of donor memory T lymphocytes directed specifically against immunodominant viral antigens has been shown to control ongoing viral infections, we designed a French

TABLE I. Patients' characteristics

Patient	Age (y)/sex	Diagnosis	Donor (MM)	GvHD grade*	GvHD treatment	Days between HSCT and first injection	CD3/μL before T-cell injection
P1	3/F	FLH	Mother (3/6)	II	Steroids 0.5 mg/kg/d aR-IL2	46	NA
P2	1.08/M	SCID T−B+NK+	Father (3/6)	—		105	127
P3	2/F	LH	Mother (3/6)	—		182	1066
P4	46/M	Blastic CML	Sibling donor (10/10)	II	Steroids 0.4 mg/kg/d	128	73
P5	2/F	AA	Sibling donor (10/10)	—		97	109
P6	0.66/F	FLH	MUD (10/10)	—		78	24
P7	52/M	CLL	Sibling donor (10/10)	II	Steroids 0.4 mg/kg/d CsA 150 mg/d	286	1831
P8	0.50/M	FLH	Mother (2/6)	—		29	0
P9	56/M	AA	MUD (10/10)	—		87	80
P10	33/M	AA	Sibling donor (10/10)	—		117	324
P11	63/F	HL	MUD (10/10)	I	Steroids 1 mg/kg/d CsA 100 mg/d	58	174
P12	1.33/M	CID	MUD (10/10)	I	Steroids 0.5 mg/kg/d MMF 270 mg/d	74	708
P13	58/M	IAL	MUD (9/10)	—		370	2300
P14	24/F	AML	MUD (9/10)	—		160	378
P15	1.66/F	AA	Mother (3/6)	—		48	0

All the HLA-partially mismatched grafts from related donors were T-cell–depleted by CD34+ immunoselection.
AA, Aplastic anemia; *AML*, acute myeloid leukemia; *CID*, combined immunodeficiency; *CLL*, chronic lymphoid leukemia; *CML*, chronic myeloid leukemia; *CsA*, cyclosporine A; *F*, female; *FLH*, familial lymphohistiocytosis; *HL*, Hodgkin lymphoma; *IAL*, immunoangioblastic lymphoma; *M*, male; *MM*, mismatch; *MMF*, mycophenolate mofetyl; *MUD*, matched unrelated donor; *NA*, not available; *P*, patient; *SCID*, severe combined immunodeficiency.
*Grade at the time of T-cell injection. The treatment is described in the next column.

multicenter pilot trial (Clinicaltrials.gov: NCT01325636) with the aim of treating pediatric or adult recipients of allogeneic HSCT (regardless of the underlying disease).[6-8] Inclusion criteria were as follow: (1) donor chimerism 10% or more at inclusion; (2) biological signs of infection with CMV with resistance or intolerance to conventional antiviral treatments, or CMV or ADV disease with documented organ damage; (3) graft versus host activity (≤II) controlled by corticoids (<1 mg/kg) at the time of inclusion; and (4) donor with positive CMV and/or ADV serology. Donor mononuclear cells were obtained by leukapheresis and were stimulated with Peptivator pp65 CMV antigen or PepAdV5 Hexon ADV antigen (both from Miltenyi Biotech, Bergisch Gladbach, Germany) for 4 and 6 hours, respectively. Magnetic enrichment of IFN-γ–secreting cells was performed with the Cytokine Secretion System and the CliniMACS device (Miltenyi Biotech). This rapid (<24 hours) and HLA-independent procedure for immunoselection has been described elsewhere in detail.[9] The virus-specific T cells (release criteria ≥ 10% IFN-γ^+ T cells) were infused immediately after the isolation procedure. This study was approved by the local institutional review board (CPP 2010-01-04) and the *Agence Nationale de Sécurité du Médicament* (reference TC271).

Between September 2010 and September 2013, 16 allogeneic HSCT recipients (8 adults and 8 infants) infected with CMV (n = 7), ADV (n = 5), or both (n = 3) were enrolled by 7 French hospitals. One CMV-infected adult withdrew his consent before treatment and was excluded from the analyses. Characteristics of treated patients are detailed in Tables I and II. Characteristics of the cell products infused are detailed in Tables E1 and E2 in this article's Online Repository at www.jacionline.org. In the CMV group, patients received 1 (n = 4), 2 (n = 5), or 3 (n = 1) anti-CMV T-cell infusions. In the ADV group, patients received 1 (n = 5), 2 (n = 2), or 3 (n = 1) anti-ADV T-cell infusions (Table E1). The median (range) time between HSCT and T-cell injection was 100.5 days (29-370 days) for patients with CMV infections and 73 days (29-159 days) for patients with ADV infections. The median (range) number of injected anti-CMV and anti-ADV CD3/IFN-γ^+ cells per kg body weight were 3,540 (1,640-19,900) and 3,739.5 (807-10,800), respectively.

Among the 10 patients with CMV infection, patient 6 died from alveolar hemorrhage before the day+21 evaluation. Patients 2, 3, and 7 showed a complete virological response after 1 (n = 2) or 2 (n = 1) infusions. This response was associated with *in vivo* expansion of CMV-specific T lymphocytes as IFN-γ–producing T cells and pentamer$^+$ CD8$^+$ T cells increased from 5.8/μL (0-13.9) (n = 7) and 1.2/μL (0-2.8) (n = 4) on the day of infusion to 20.58/μL (0.16-49.1) and 3.2/μL (0.4-7.6) at day+21,

TABLE II. Follow-up and outcomes of patients after the adoptive transfer of CMV- and ADV-specific T cells

Patient	Infection	Viral load at day+0 (log/mL)	Viral load at day+21 (log/mL)	GvHD grade at day+21	CD3+ specific T-cell expansion at day+21	Clinical outcome 6 mo after the first injection/ cause of death
CMV-infected patients						
P2	Meningoencephalitis Retinitis	2.5	<threshold	None	Yes	Alive with stabilization of retinitis
P3	Diarrhea Retinitis Blood replication	4.2	<threshold	None	Yes	Alive with stabilization of retinitis
P5	Blood replication	2.4	3.3	None	No	Alive/death at day+186/viral cardiorespiratory failure
P6*	Pneumopathy Encephalitis Retintis Blood replication	3.7	NA	NA	NA	Death at day+3/alveolar hemorrhage
P7	Blood replication	2.3	4.3	None	Yes	Alive with extensive cGvHD
P8	Blood replication	5.8	5.7	None	No	Death at day+96/pulmonary arterial hypertension
P10	Pneumopathy Blood replication	3.8	4.1	Grade III	Yes	Death at day+97/ADV pneumonitis
P12	CMV retinitis	4.5	NA	None	Yes	Alive and blind
P13	Blood replication	3.6	4.1	None	Yes	Alive and well
P15	Diarrhea	5.8	6.5	None	No	Death at day+30/disseminated ADV and CMV infection
ADV-infected patients						
P1	Meningoencephalitis Retinitis	2.5	<threshold	None	Yes	Alive with stabilization of retinitis
P4	Diarrhea Retinitis Blood replication	4.2	*P* < threshold	None	Yes	Alive with stabilization of retinitis
P5	Blood replication	2.4	3.3	None	No	Alive/death at day+186/viral cardiorespiratory failure
P8	Pneumopathy Encephalitis Retintis Blood replication	3.7	NA	NA	NA	Death at day+3/alveolar hemorrhage
P9†	Blood replication	2.3	4.3	None	Yes	Alive
P11	Blood replication	5.8	5.7	None	No	Death at day+25/alveolar hemorrhage
P14	Pneumopathy Blood replication	5.4	Positive <threshold	None	Yes	Death at day+33/PTLD
P15‡	Diarrhea Blood replication	5.8	NA	NA	NA	Death at day+30/disseminated ADV and CMV infection

Threshold of detection was 500 copies of infectious genome per milliliter for ADV and CMV quantitative PCR.
CGvHD, Chronic graft versus host disease; *NA*, not available; *P*, patient; *PTLD*, posttransplant lymphoproliferative disease.
*P6 died 3 days after adoptive transfer.
†P9 died 14 days after adoptive transfer.
‡P15 died 3 days after adoptive transfer.

respectively. Remarkably, the T-cell infusion allowed the complete remission of CMV encephalitis in patient 2 (Fig 1, *A*). Five patients did not display any significant changes in CMV viral load at day+21. The lack of *in vivo* CMV-specific T-cell expansion at day 21 was always associated with the absence of an anti-CMV response. Clinical evaluation 6 months after the last injection showed that only 1 patient among 3 (patient 15) had died from a CMV-related disease (Table II).

Among the 8 patients with ADV infection, patients 9 and 15 died before the day+21 evaluation. Of the remaining 5 patients, 3 showed a complete virological response at day+21, 1 a partial response (that became complete at day+47), and 1 no response. Two of the 4 patients with virological response (patients 4 and 14) also displayed ADV-specific T-lymphocytes expansion. The clinical outcome was unfavorable in all but 1 patient with ADV but only 1 of the deaths was related to ADV (patient 1) (Table II).

A total of 9 severe adverse events (SAEs) occurred in 6 patients and were classified as having a possible link with T-cell infusion. Four ADV-infected patients experienced worsening of respiratory symptoms or liver cytolysis that could be related to the natural course of the infection, another viral infection, or a proper T-cell infusion effect. Two patients presented with apparent septic shock following the infusion while the microbiological testing result of the T-cell product was negative. Other SAEs were grade III graft

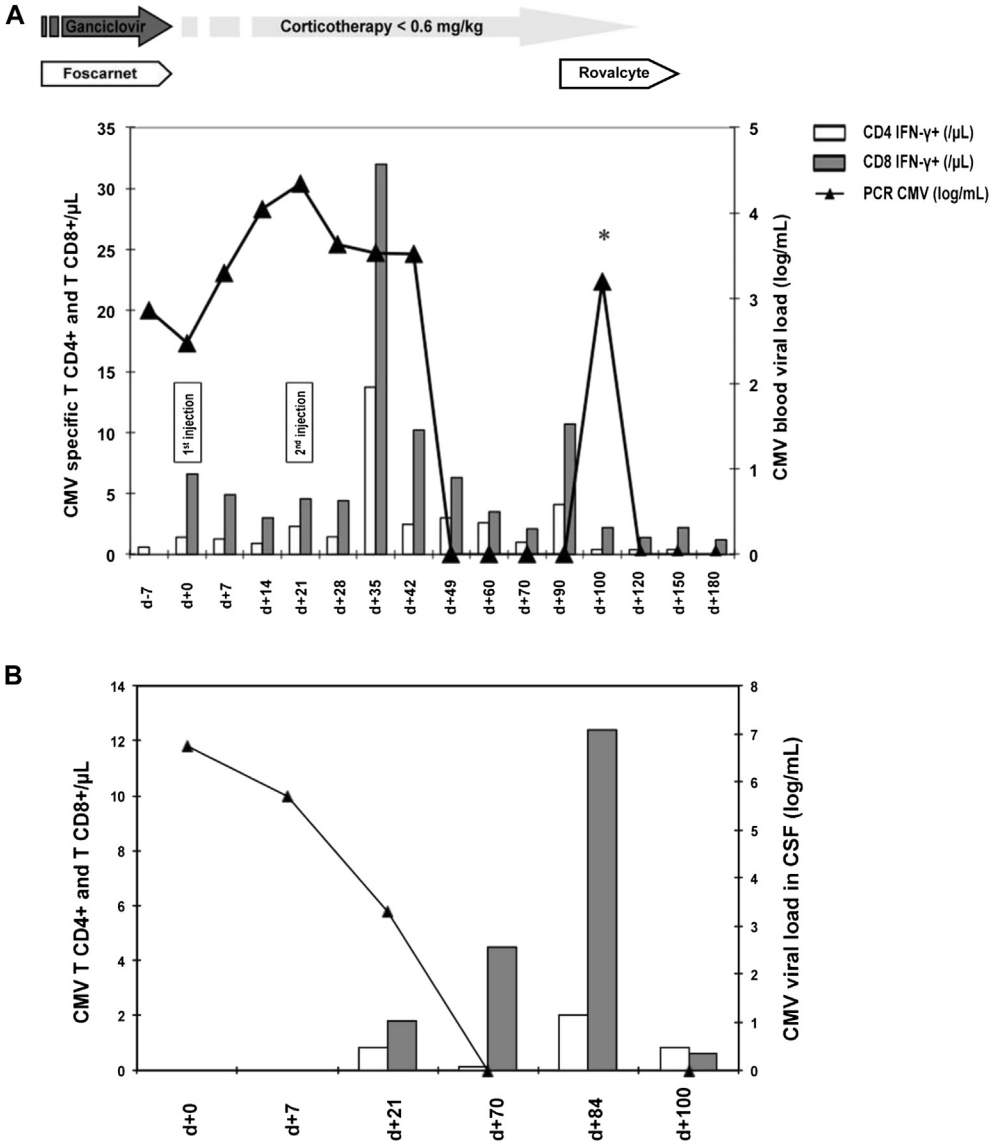

FIG 1. Evolution of viral load and circulating CD4 and CD8 IFN-γ+ T-cell counts after antiviral adoptive therapy in patient 7 **(A)** and patient 2 **(B)**. In patient 7, the regression of the viral load was concomitant with a significant and intentional reduction of corticosteroids to 5 mg (total dose), whereas the viral reactivation at d+100 was concomitant to a worsening of chronic graft versus host disease requiring corticosteroids additional increase up to 0.5 mg/kg. *Viral load at day 100 was measured by the local laboratory but was not recorded in the study database. *CSF,* Cerebrospinal fluid.

versus host disease (n = 1), CMV reactivation (n = 1), and hematemesis (n = 1) (see Table E3 in this article's Online Repository at www.jacionline.org).

Despite the relatively low number of patients included, this study shows that rapidly prepared CMV- and/or ADV-specific T cells seem efficient in a subset of HSCT recipients with severe viral infections as one-third of the patients showed a complete virological response in parallel with specific T-cell expansion even in the presence of significant corticotherapy. The cell infusion seems to be safe despite the difficulty in accurately assessing SAEs in an observational study of patients with extremely poor condition at inclusion. However, larger studies are needed to assess clinical and biological parameters associated with treatment failure and efficacy. Moreover, as timing and dosage of the treatment might have a major influence on efficacy, future works should investigate the optimal timing of infusion —with consideration with preemptive therapy—and the optimal cell dose to infuse—with regard to the risk of graft versus host disease induction.

We thank the patients and the parents of pediatric patients who participated in this study. We also thank the Clinical Research Unit at Necker Children's Hospital and particularly Valérie Jolaine and Elodie Henry for their investment.

Rita Creidy, PharmD, PhD[a]
Despina Moshous, MD, PhD[b,c]
Fabien Touzot, MD, PhD[a,b,d]
Caroline Elie, MD, PhD[e]

Bénédicte Neven, MD, PhD[b,c]
Aurélie Gabrion, MSc[a]
Marianne Leruez-Ville, MD, PhD[f,g]
Sébastien Maury, MD, PhD[h,i]
Brigitte Ternaux, PGDipMLSc[a]
Jennifer Nisoy, PGDipMLSc[a]
Jean-Marc Luby, PGDipMLSc[a]
Sébastien Héritier, MD, PhD[b]
Jean-Hugues Dalle, MD, PhD[j,k]
Marie Ouachée-Chardin, MD, PhD[j]
Aliénor Xhaard, MD[l]
Xavier Thomas, MD, PhD[m]
Patrice Chevallier, MD, PhD[n]
Laetitia Souchet, MD[o]
Jean-Marc Treluyer, MD, PhD[e]
Capucine Picard, MD, PhD[p]
Salima Hacein-Bey-Abina, PharmD, PhD[a,q,r,s]
Liliane Dal Cortivo, MD[a]
Stéphane Blanche, MD[g,t]
Marina Cavazzana, MD, PhD[a,b,d]

From [a]the Biotherapy Department, Necker Children's Hospital, Assistance Publique-Hôpitaux de Paris, Paris, France; [b]the Immunology and Pediatric Hematology Department, Necker Children's Hospital, Assistance Publique-Hôpitaux de Paris, Paris, France; [c]Genome Dynamics in the Immune System-INSERM UMR1163, Paris Descartes-Sorbonne Paris Cité University, Imagine Institute, Paris, France; [d]Human Lymphohematopoiesis-INSERM UMR1163, Paris Descartes-Sorbonne Paris Cité University, Imagine Institute, Paris, France; [e]the Clinical Reaserch Unit, Center of Clinical Investigation, Necker Children's Hospital, Assistance Publique-Hôpitaux de Paris, Paris, France; [f]the Clinical Microbiology Laboratory, National Reference Center for Cytomegalovirus, Necker Children's Hospital, Assistance Publique-Hôpitaux de Paris, Paris, France; [g]Paris Descartes-Sorbonne Paris Cité University, Paris, France; [h]the Hematology Department, Henri Mondor's Hospital, Assistance Publique-Hôpitaux de Paris, Créteil, France; [i]DHU Virus-Immunity-Cancer, Paris Est Créteil University (UPEC), Créteil, France; [j]the Pediatric Hematology Department, Robert Debré's Hospital, Assistance Publique-Hôpitaux de Paris, Paris, France; [k]Equipe "Immunité chez l'enfant"-INSERM UMR1149, Université Paris Diderot, Robert Debré's Hospital, Paris, France; [l]the Hematology Department, Hematopoietic Stem Cell Transplantation Unit, Saint-Louis's Hospital, Assistance Publique-Hôpitaux de Paris, Paris, France; [m]Hematology Department, Lyon-Sud's Hospital, Groupement Hospitalier Sud, Lyon, France; [n]Hematology Department, Centre Hospitalier-Universitaire Hotel-Dieu, Nantes, France; [o]Hematology Department, La Pitié Salpétrière's Hospital, Assistance Publique-Hôpitaux de Paris, Paris, France; [p]Centre d'Étude des Déficits Immunitaires (CEDI), Necker Children's Hospital, Assistance Publique-Hôpitaux de Paris, Paris, France; [q]Faculté des Sciences Pharmaceutiques et Biologiques, Paris Descartes-Sorbonne Paris Cité University, Imagine Institute, Paris, France; [r]the Biotherapy Clinical Investigation Center, Groupe Hospitalier Universitaire Ouest, Assistance Publique-Hôpitaux de Paris, INSERM, Paris, France; [s]the Immunology Laboratory, Groupe Hospitalier Universitaire Paris-Sud, Assistance Publique-Hôpitaux de Paris, Le Kremlin Bicêtre, France; and [t]Pediatric Hematology Department, Immunology Unit, Necker Children's Hospital, Assistance Publique-Hôpitaux de Paris, Paris, France. E-mail: m.cavazzana@nck.aphp.fr.

This work was supported by "Programme Hospitalier de Recherche Clinique" (PHRC national 2010 00-13) of the Health Ministry, Assistance Publique-Hôpitaux de Paris, and the Direction de la Recherche Clinique et du Développement.

Disclosure of potential conflict of interest: M. Leruez-Ville has received research support from the Direction de la Recherche Clinique et du Développement and has received travel support from Biomerieux and Diasorin. J.-H. Dalle is on the boards for Jazz Pharmaceuticals, Astellas, Novartis, Biotest, Macropharma, and Chimerix; has received research support from Sanofi; has received lecture fees, travel support, and payment for developing educational presentations from Jazz Pharmaceuticals; and has received travel support from Pierre Fabre Medicaments. The rest of the authors declare that they have no relevant conflicts of interest.

REFERENCES

1. Hiwarkar P, Gaspar HB, Gilmour K, Jagani M, Chiesa R, Bennett-Rees N, et al. Impact of viral reactivations in the era of pre-emptive antiviral drug therapy following allogeneic haematopoietic SCT in paediatric recipients. Bone Marrow Transplant 2013;48:803-8.
2. Handgretinger R, Chen X, Pfeiffer M, Schumm M, Mueller I, Feuchtinger T, et al. Cellular immune reconstitution after haploidentical transplantation in children. Biol Blood Marrow Transplant 2008;14:59-65.
3. Einsele H, Mielke S, Grigoleit GU. Diagnosis and treatment of cytomegalovirus 2013. Curr Opin Hematol 2014;21:470-5.
4. Lindemans CA, Leen AM, Boelens JJ. How I treat adenovirus in hematopoietic stem cell transplant recipients. Blood 2010;116:5476-85.
5. Salzberger B, Bowden RA, Hackman RC, Davis C, Boeckh M. Neutropenia in allogeneic marrow transplant recipients receiving ganciclovir for prevention of cytomegalovirus disease: risk factors and outcome. Blood 1997;90:2502-8.
6. Walter EA, Greenberg PD, Gilbert MJ, Finch RJ, Watanabe KS, Thomas ED, et al. Reconstitution of cellular immunity against cytomegalovirus in recipients of allogeneic bone marrow by transfer of T-cell clones from the donor. N Engl J Med 1995;333:1038-44.
7. Feuchtinger T, Matthes-Martin S, Richard C, Lion T, Fuhrer M, Hamprecht K, et al. Safe adoptive transfer of virus-specific T-cell immunity for the treatment of systemic adenovirus infection after allogeneic stem cell transplantation. Br J Haematol 2006;134:64-76.
8. Icheva V, Kayser S, Wolff D, Tuve S, Kyzirakos C, Bethge W, et al. Adoptive transfer of Epstein-Barr virus (EBV) nuclear antigen 1-specific t cells as treatment for EBV reactivation and lymphoproliferative disorders after allogeneic stem-cell transplantation. J Clin Oncol 2013;31:39-48.
9. Feuchtinger T, Lang P, Hamprecht K, Schumm M, Greil J, Jahn G, et al. Isolation and expansion of human adenovirus-specific CD4+ and CD8+ T cells according to IFN-gamma secretion for adjuvant immunotherapy. Exp Hematol 2004;32:282-9.

Available online April 30, 2016.
http://dx.doi.org/10.1016/j.jaci.2016.03.032

A combination of dexamethasone and anti–IL-17A treatment can alleviate diesel exhaust particle–induced steroid insensitive asthma

To the Editor:

A recent comprehensive and systematic review of worldwide traffic emissions and health science by a special panel convened by the Health Effects Institute found sufficient evidence that exposure to traffic-related air pollution (TRAP) causes asthma exacerbation in children.[1] Diesel exhaust particles (DEPs) represent the major component of TRAP particulate matter and the main contributor to TRAP-related asthma exacerbations in children. We have previously shown that in children with allergic asthma, TRAP exposure is associated with earlier sensitization, and increased asthma prevalence and severity.[2,3] *Asthma severity*, defined as more frequent weekly symptoms, was associated with increased IL-17A but not IL-4, IL-5, or IL-13 blood levels.[2] Indeed, although asthma has long been described as a disease resulting from an abnormal T_H2 immune response to environmental allergens, accumulating evidence suggests a role for T_H17 cells, especially in severe asthma.[4] A recent study demonstrated that dual-positive T_H2/T_H17 cells and IL-17A were present at a higher frequency in the bronchoalveolar lavage fluid (BALF) of patients with severe asthma.[5] Furthermore, the study found that these T_H2/T_H17 cells were resistant to dexamethasone-induced cell death. We recently reported that DEP coexposure augmented allergen-induced airway hyperresponsiveness (AHR), eosinophilia, and T_H2 and T_H17 cytokines levels, and resulted in increased numbers of T_H2/T_H17 cells in the BALF.[2] Collectively, these data suggest that a subgroup of patients with asthma with high DEP exposure and mixed T_H2/T_H17 responses may benefit from anti–IL-17A therapy alone or in combination with steroids. Although inhibition of IL-17 receptor A did not result in significant improvement among subjects with moderate to severe asthma in a recent randomized controlled trial,[6] targeted anti–IL-17 therapy in a subset

TABLE E1. Characteristics of CMV-specific T cells

Patient	No. of procedures	No. of infusions	% of IFN-γ+ cells/ CD3+ lymphocytes	CD4+IFN-γ+ count (10^4)	CD8+IFN-γ+ count (10^4)	Yield of IFN-γ+ CD4+ T cell (%)	Yield of IFN-γ+ CD8+ T cell (%)	Dose of IFN-γ+ CD3+/kg
P2	1	2	23.8	15.00	28.00	54	85	5,113 4,938
P3	1	2	92.5	16.00	112.00	70	80	5,000 5,000
P5	1	1	22.4	0.79	0.76	19	35	2,280
P6	1	1	18	0.98	0.39	0.9	1	1,760
P7	1	2	95.8	110.00	3.24	18	4	5,428 15,100
P8	1	3	93.3	34.80	219.00	46	49	3,030 5,880 19,900
P10	1	1	96.4	12.40	83.80	16	15	1,640
P12	1	1	96.1	0.39	4.99	2.4	12	4,950
P13	1	1	86.4	8.60	37.60	22	30	4,800
	2	1	85.4	6.36	31.80	48	55	5,127
P15	1	2	96.3	41.20	250.00	72	83	5,000 5,000
Median			92.50	12.40	31.80	22.00	35.00	3,540.00

P, Patient.

TABLE E2. Characteristics of ADV-specific T cells

Patient	No. of procedures	No. of infusions	% of IFN-γ+ cells/ CD3+ lymphocytes	CD4+IFN-γ+ count (10^4)	CD8+IFN-γ+ count (10^4)	Yield of IFN-γ+ CD4+ T cell (%)	Yield of IFN-γ+ CD8+ T cell (%)	Dose of IFN-γ+ CD3+/kg
P1	1	2	33.5	7.81	8.20	4	5	5,000 1,546
P4	1	1	59	17.15	38.66	13	14	3,979
P5	1	1	39	0.52	0.22	0.6	0.3	1,167
	2	1	28	1.31	0.93	7	5	3,298
	3	1	18.6	7.67	5.89	31	23	10,800
P8	1	2	89.7	46.50	63.80	83	12	2,970 5,210
P9	1	1	77.4	14.70	16.80	166	82	3,500
P11	1	1	79.7	0.66	0.68	5	4	807
P14	1	1	80.4	28.00	93.80	73	88	5,140
P16	1	1	63.8	3.15	9.30	42	47	5,000
Median			61.40	7.74	8.75	22.00	13.00	3,739.50

P, Patient.

TABLE E3. Serious adverse event observed in treated patients

Patient	SAE	Delay between SAE and specific T-cell infusion
P1	Multivisceral failure due to disseminated CMV infection Death	Day+7 Day+31
P2	None	NA
P3	None	NA
P4	Sepsis	Day+1
P5	Worsening respiratory symptoms	5 mo
P6	Alveolar hemorrhage and death	Day+3
P7	Gram-negative sepsis	Day+12
P8	Pulmonary hypertension and intraalveolar hemorrhage Death	Day+36 Day+96
P9	Multivisceral failure Death	Day+10 Day+14
P10	Stage III GvHD Death from ADV pneumonitis	Day+5 Day+97
P11	Intraalveolar hemorrhage, hematemesis Death	Day+14 Day+25
P12	None	NA
P13	Sepsis Pneumopathy	Day+23 Day+48
P14	Respiratory distress Death from PTLD	Day+20 Day+33
P15	Acute respiratory distress syndrome due to CMV and ADV and death	Day+3

GvHD, Graft versus host disease; *NA*, not applicable; *P*, patient; *PTLD*, posttransplant lymphoproliferative disease.