hemifacial spasm. The dysphagia, dysarthria, and ptosis had fully resolved, and his percutaneous endoscopic gastrostomy tube was removed.

Discussion. Despite the rarity of neurotoxicity secondary to checkpoint inhibitor therapies, it must be considered in all patients with previous exposure who present with a new neurologic deficit. Immune-related neurotoxicity remains a diagnosis of exclusion; it requires ruling out brain metastases, infection, and paraneoplastic syndromes. However, a timely diagnosis is crucial. As illustrated by our case, nivolumab-induced neurotoxicity can be both life-threatening and reversible with the appropriate treatment. Although the exact mechanism of nivolumab-induced cranial neuropathy is unknown, this case suggests that treatment with corticosteroids alone may be insufficient, at least in severe cases, and that the addition of plasmapheresis and intravenous immunoglobulin can lead to sustained recovery.

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1. El-Khoueiry AB, Sangro B, Yau T, et al. Nivolumab in patients with advanced hepatocellular carcinoma (CheckMate 040): an open-label, non-comparative, phase 1/2 dose escalation and expansion trial. *Lancet*. 2017. 2017;389(10088):2492-2502.
2. US Food and Drug Administration. FDA grants accelerated approval to nivolumab for HCC previously treated with sorafenib [news release]. US Food and Drug Administration website. https://www.fda.gov/Drugs/InformationOnDrugs/ApprovedDrugs/ucm577166.htm. Updated September 25, 2017. Accessed October 24, 2017.
3. Bristol-Myers Squibb. A Randomized, Multi-center Phase III Study of Nivolumab Versus Sorafenib as First-Line Treatment in Patients With Advanced Hepatocellular Carcinoma (CheckMate 459: CHECKpoint Pathway and nivoluMAb Clinical Trial Evaluation 459). ClinicalTrials.gov Identifier: NCT02576509. ClinicalTrials.gov website. https://clinicaltrials.gov/ct2/show/NCT02576509. Accessed October 24, 2017.
4. Touat M, Talmasov D, Ricard D, Psimaras D. Neurological toxicities associated with immune-checkpoint inhibitors. *Curr Opin Neurol*. 2017; 30(6):659-668.
5. Daiichi Sankyo, Inc. A Phase 3, Randomized, Double-Blind Study of Tivantinib (ARQ 197) in Subjects With MET Diagnostic-High Inoperable Hepatocellular Carcinoma Treated With One Prior Systemic Therapy. ClinicalTrials.gov Identifier: NCT0175576. ClinicalTrials.gov website. https://clinicaltrials.gov/ct2/show/NCT01755767. Accessed November 20, 2017.

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Statin Use Associated With a Decreased Risk of Community-Acquired *Staphylococcus aureus* Bacteremia

To the Editor: We read with great interest the recent article by Smit et al[1] on statin use associated with a decreased risk of community-acquired *Staphylococcus aureus* bacteremia (CA-SAB), particularly in patients with chronic kidney disease and patients with diabetes. They explained that these results were unlikely due to direct antimicrobial effects of statins on *S aureus* but more likely due to the pleiotropic effects of statins reducing important isoprenoid intermediates, resulting in decreased bacterial invasion and inducing neutrophil extracellular traps.

By reviewing the available literature of statins' in vitro antibacterial effects, we observed that simvastatin, followed by atorvastatin, generally exerted the greatest direct antibacterial effect (lowest minimum inhibitory concentration) against *S aureus* compared with other statins.[2] This finding supports the view that direct antimicrobial effects were unlikely responsible for statins' protective effects because Smit et al have provided complementary evidence that the risk of contracting CA-SAB was higher, rather than lower, in patients taking simvastatin or atorvastatin compared with the other statins.[1] As such, it is more probable that statins reduce CA-SAB risk through other host-related mechanisms.

Interestingly, a recent study by Plotkin and Konakieva[3] found that steroid hormones with the 3-hydroxy moiety (eg, cholesterol and estradiol) increased carotenoid levels in *S aureus*, which potentially increases bacterial virulence.[4] Patients with chronic kidney disease usually have low levels of sex steroid hormones,[5] but high levels of estradiol may present in septic patients.[6] Knowledge of the antibiotic treatment outcomes for patients with chronic kidney who have CA-SAB and are statin users, compared with nonusers, might provide clues as to whether statins could offer additional benefits by suppressing the antagonistic precursor cholesterol molecule and downstream steroidal hormones sufficiently, resulting in efficacious antibiotic therapy.

Because statins may induce new-onset diabetes and the colonization of skin and mucosae with *S aureus* predisposes diabetic patients to infections,[7,8] statin users with diabetes might be expected to have a higher risk of CA-SAB. However, the results of Smit et al[1] revealed otherwise. Other conflicts yet to be reconciled include opposing evidence that statins do not produce neutrophil extracellular trap production[9] or why meta-analysis of clinical trials examining the outcome of statins in septic patients differ.[10,11] In addition, when statins influence the human gut microbiota[12] or activate nuclear receptors,[13] the resultant impact to the human immune system has not been elucidated.

The work of Smit et al is interesting and timely and should stimulate further investigation into the role of statins in preventing bacteremia.

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1. Smit J, López-Cortés LE, Thomsen RW, et al. Statin use and risk of community-acquired *Staphylococcus aureus* bacteremia: a population-based

case-control study. *Mayo Clin Proc*. 2017;92(10):1469-1478.
2. Ko HHT, Lareu RR, Dix BR, Hughes JD. Statins: antimicrobial resistance breakers or makers? *PeerJ*. 2017;5:e3952.
3. Plotkin BJ, Konakieva MI. Attenuation of antimicrobial activity by the human steroid hormones. *Steroids*. 2017;128:120-127.
4. Liu GY, Nizet V. Color me bad: microbial pigments as virulence factors. *Trends Microbiol*. 2009;17(9):406-413.
5. Meuwese CL, Carrero JJ. Chronic kidney disease and hypothalamic-pituitary axis dysfunction: the chicken or the egg? *Arch Med Res*. 2013;44(8):591-600.
6. Fourrier F, Jallot A, Leclerc L, et al. Sex steroid hormones in circulatory shock, sepsis syndrome, and septic shock. *Circ Shock*. 1994;43(4):171-178.
7. Weintrob AC, Sexton DJ. Susceptibility to infections in persons with diabetes mellitus. UpToDate website. http://www.uptodate.com/contents/susceptibility-to-infections-in-persons-with-diabetes-mellitus. Updated December 5, 2016. Accessed November 2, 2017.
8. Betteridge DJ, Carmena R. The diabetogenic action of statins—mechanisms and clinical implications. *Nat Rev Endocrinol*. 2016;12(2):99-110.
9. Sørensen OE, Borregaard N. Neutrophil extracellular traps—the dark side of neutrophils. *J Clin Invest*. 2016;126(5):1612-1620.
10. Janda S, Young A, Fitzgerald JM, Etminan M, Swiston J. The effect of statins on mortality from severe infections and sepsis: a systematic review and meta-analysis. *J Crit Care*. 2010;25(4). 656.e7-656.e22.
11. Deshpande A, Pasupuleti V, Rothberg MB. Statin therapy and mortality from sepsis: a meta-analysis of randomized trials. *Am J Med*. 2015;128(4):410-417.e1.
12. Zhernakova A, Kurilshikov A, Bonder MJ, et al. Population-based metagenomics analysis reveals markers for gut microbiome composition and diversity. *Science*. 2016;352(6285):565-569.
13. Howe K, Sanat F, Thumser AE, Coleman T, Plant N. The statin class of HMG-CoA reductase inhibitors demonstrate differential activation of the nuclear receptors PXR, CAR and FXR, as well as their downstream target genes. *Xenobiotica*. 2011;41(7):519-529.

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In Reply—Statin Use Associated With a Decreased Risk of Community-Acquired *Staphylococcus aureus* Bacteremia

We appreciate Dr Ko and colleagues' interesting reflections on our findings concerning the influence of statin use on the risk of community-acquired *Staphylococcus aureus* bacteremia (CA-SAB). Because the aim of our study was to provide epidemiological in vivo data on this association, Ko and colleagues' review of the literature and considerations on the potential underlying pathophysiologic mechanisms constitute a very valuable supplement to our paper. We agree that the risk of CA-SAB appeared to differ slightly across the different types of statins (simvastatin, atorvastatin, and others). However, because only 9% of current statin users were treated with other statins and because the confidence intervals for the estimates overlapped, these results should be interpreted with caution.

As suggested in the letter by Ko et al, we believe that future well-conducted basic and clinical research represents the only way to disentangle the biological mechanisms by which statin treatment may protect against CA-SAB.

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Potential Competing Interests: Dr Nielsen serves on the advisory boards of Gilead Sciences, Inc, AbbVie Inc, and Bristol-Myers Squibb Company. Dr López-Cortés has received payments for lectures and development of educational presentations from Merck Sharp & Dohme Corp and Angelini Acraf S.p.A. Dr Rodríguez-Baño has received payments from Merck Sharp & Dohme Corp for development of educational presentations and from AstraZeneca for coordinating a research project.

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Daratumumab for POEMS Syndrome

To the Editor: The syndrome of polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, and skin changes (POEMS) is a rare disorder. It is considered paraneoplastic to a usually IgAλ-secreting monoclonal plasma cell dyscrasia.[1] High-dose melphalan followed by autologous stem cell transplant (ASCT) is the standard of care in disseminated POEMS syndrome but can be associated with significant treatment-related morbidity and mortality.[2] No paradigm exists for managing patients who experience relapse and those ineligible for ASCT. Herein, we report the first case of POEMS syndrome treated successfully with the anti-CD38 monoclonal antibody daratumumab and lenalidomide.

Report of Case. A 60-year-old woman presented with a progressive sensorimotor polyneuropathy, weight loss, and acrocyanosis of the distal extremities and nose. Laboratory evaluation revealed an IgAλ monoclonal band of 0.7 g/dL and elevated serum IgA (689 mg/dL). The λ and κ free light chain levels were 10.3 mg/dL and 3.7 mg/dL, respectively (Supplemental Table, available online at http://www.mayoclinicproceedings.org). Bone marrow biopsy studies revealed 5% to 10% plasma cells with 0.59% myelomatous cells. The vascular endothelial growth factor (VEGF) level was 2222 pg/mL, and the platelet count was 572 × 10^9/L. Imaging identified no bone disease or organomegaly. POEMS syndrome was diagnosed. Prior treatment with intravenous