in the Supplementary Appendix). We performed this follow-up testing because, in the index case reported by Seikrit et al.,[3] the patient had anti–factor H antibodies that appeared a few months after diagnosis, concomitant with renal-disease progression and with the disappearance of anti-PLA_2R antibodies. However, we did not detect anti–factor H antibodies in any patients during follow-up (Fig. 1C). We confirmed the results by means of Western blot assay in selected patients (Fig. S1 and Tables S1 and S2).

Taken together, our data do not support the hypothesis that anti–factor H antibodies might contribute to hyperactivation of the alternative pathway and accelerate disease progression in membranous nephropathy. However, the presence of anti–factor H antibodies in very exceptional cases cannot be ruled out.

Elisabetta Valoti, Ph.D.
Marina Noris, Ph.D.
Giuseppe Remuzzi, M.D.
Istituto di Ricerche Farmacologiche Mario Negri IRCCS
Bergamo, Italy

1. Beck LH Jr, Bonegio RG, Lambeau G, et al. M-type phospholipase A2 receptor as target antigen in idiopathic membranous nephropathy. N Engl J Med 2009;361:11-21.
2. Bally S, Debiec H, Ponard D, et al. Phospholipase A2 receptor-related membranous nephropathy and mannan-binding lectin deficiency. J Am Soc Nephrol 2016;27:3539-44.
3. Seikrit C, Ronco P, Debiec H. Factor H autoantibodies and membranous nephropathy. N Engl J Med 2018;379:2479-81.
4. Ruggenenti P, Debiec H, Ruggiero B, et al. Anti-phospholipase A2 receptor antibody titer predicts post-rituximab outcome of membranous nephropathy. J Am Soc Nephrol 2015;26:2545-58.
5. Watson R, Lindner S, Bordereau P, et al. Standardisation of the factor H autoantibody assay. Immunobiology 2014;219:9-16.

Ribociclib and Endocrine Therapy in Breast Cancer

TO THE EDITOR: The MONALEESA-7 (Mammary Oncology Assessment of LEE011's [Ribociclib's] Efficacy and Safety–7) trial (July 25 issue)[1] showed a significant overall survival benefit with the addition of a cyclin-dependent kinase 4 and 6 (CDK4/6) inhibitor, ribociclib, to endocrine therapy in patients with luminal advanced breast cancer. In the PALOMA-3 (Palbociclib: Ongoing Trials in the Management of Breast Cancer–3) trial,[2] however, palbociclib added to fulvestrant did not improve overall survival significantly. A higher percentage of patients in the MONALEESA-7 trial (which focused on first-line therapy) had endocrine-sensitive disease[1] or were of Asian race (approximately 30%, vs. 20% in the PALOMA-3 trial),[3] both of which are factors that may have contributed to the difference in outcomes.

Only 73% of the patients in the placebo group in the MONALEESA-7 trial received further lines of therapy, which is somewhat unexpected in this population of young patients, most of whom (86%) received the study treatment as first-line treatment.[4] In comparison, 80% of the patients in the placebo group in the PALOMA-3 trial received at least one additional line of therapy, although most patients (75%) received the study treatment as a second-line or later line of treatment.[2] We wonder if the extent of subsequent treatments may have affected overall survival, given the documented effect of survival after disease progression on the ability to detect an overall survival benefit.[5]

Andrea Rocca, M.D.
Elisabetta Melegari, M.D.
Michela Palleschi, M.D.
Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST) IRCCS
Meldola, Italy
andrea.rocca@irst.emr.it

Dr. Rocca reports having served on advisory boards for Novartis, Pfizer, and Lily. No other potential conflict of interest relevant to this letter was reported.

1. Im S-A, Lu Y-S, Bardia A, et al. Overall survival with ribociclib plus endocrine therapy in breast cancer. N Engl J Med 2019;381:307-16.
2. Turner NC, Slamon DJ, Ro J, et al. Overall survival with palbociclib and fulvestrant in advanced breast cancer. N Engl J Med 2018;379:1926-36.
3. Lee KWC, Lord S, Finn RS, et al. The impact of ethnicity on efficacy and toxicity of cyclin D kinase 4/6 inhibitors in advanced breast cancer: a meta-analysis. Breast Cancer Res Treat 2019;174:271-8.
4. Tripathy D, Im SA, Colleoni M, et al. Ribociclib plus endocrine therapy for premenopausal women with hormone-receptor-positive, advanced breast cancer (MONALEESA-7): a randomised phase 3 trial. Lancet Oncol 2018;19:904-15.
5. Broglio KR, Berry DA. Detecting an overall survival benefit that is derived from progression-free survival. J Natl Cancer Inst 2009;101:1642-9.

THE AUTHORS REPLY: Rocca et al. ask whether the proportion of patients receiving subsequent ther-

apy in the MONALEESA-7 trial could explain the overall survival results, with attenuated survival times being associated with more aggressive disease and fewer later-line treatments. They compare the subsequent therapy provided in the PALOMA-3 trial with the therapy provided in MONALEESA-7. This comparison may not be appropriate given the differences in the patient populations, particularly given the higher likelihood of endocrine sensitivity in the PALOMA-3 trial owing to the fact that patients had previously received a line of endocrine therapy, which was not the case in the MONALEESA-7 trial.[1] In the PALOMA-2 trial, which involved the evaluation of CDK4/6 inhibitors as first-line endocrine therapy, 75% of patients received subsequent therapy,[2] similar to the 71% who received subsequent therapy in MONALEESA-7.[1] Regarding the comment on specific subgroups — such as persons of Asian descent or those with endocrine sensitivity — exploratory subgroup analyses were completed to assess the overall survival consistency evident from the subgroup hazard ratios and 95% confidence intervals. Ascribing any causality on the basis of differences in individual subgroups post hoc can be problematic because there has been no adjustment for multiplicity, which may lead to spurious findings.

Seock-Ah Im, M.D., Ph.D.
Seoul National University College of Medicine
Seoul, South Korea

Yen-Shen Lu, M.D., Ph.D.
National Taiwan University Hospital
Taipei, Taiwan

Debu Tripathy, M.D.
University of Texas M.D. Anderson Cancer Center
Houston, TX
dtripathy@mdanderson.org

Since publication of their article, the authors report no further potential conflict of interest.

1. Turner NC, Slamon DJ, Ro J, et al. Overall survival with palbociclib and fulvestrant in advanced breast cancer. N Engl J Med 2018;379:1926-36.
2. Rugo HS, Finn RS, Diéras V, et al. Palbociclib plus letrozole as first-line therapy in estrogen receptor-positive/human epidermal growth factor receptor 2-negative advanced breast cancer with extended follow-up. Breast Cancer Res Treat 2019;174:719-29.

Erdafitinib in Urothelial Carcinoma

TO THE EDITOR: Erdafitinib received accelerated approval by the Food and Drug Administration (FDA) in April 2019 for the treatment of patients with advanced urothelial cancer who carried the *FGFR2/3* alterations.[1] However, it remains unclear what is the most appropriate sequencing of therapies (immunotherapy and targeted therapy). Loriot et al. (July 25 issue)[2] suggest the use of erdafitinib over immunotherapy given the better response rate, similar rates of overall survival, and lower activity of immunotherapy in patients with the *FGFR* mutation. However, we have a few concerns and think that immunotherapy may still be preferred over erdafitinib. First, *FGFR* mutation status has yet to be proven to be a biomarker for resistance to immunotherapy. Recently, a large retrospective study of immunotherapy (which included the IMVigor 210 [A Study of Atezolizumab in Participants with Locally Advanced or Metastatic Urothelial Bladder Cancer] and CheckMate 275 [Nivolumab in Metastatic Urothelial Carcinoma after Platinum Therapy] cohorts) showed similar response rates irrespective of *FGFR* mutation status.[3] Second, a longer median response (68% of patients with a response for at least 12 months) with fewer toxic effects of grade 3 or more (15% vs. 46%) suggests that immunotherapy may provide a better safety and efficacy profile than *FGFR* targeted therapy.[4] The different immunotherapy agents have shown promising activity in advanced urothelial cancer across multiple trials.

Vinod Sharma, M.D., D.M.
Ilavarasi Vanidassane, M.B., B.S., M.D.
All India Institute of Medical Sciences
New Delhi, India
vinod_mbbs4u@yahoo.co.in

No potential conflict of interest relevant to this letter was reported.

1. FDA grants accelerated approval to erdafitinib for metastatic urothelial carcinoma. Silver Spring, MD: Food and Drug Administration, April 12, 2019 (https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-erdafitinib-metastatic-urothelial-carcinoma).
2. Loriot Y, Necchi A, Park SH, et al. Erdafitinib in locally advanced or metastatic urothelial carcinoma. N Engl J Med 2019;381:338-48.
3. Wang L, Gong Y, Saci A, et al. Fibroblast growth factor receptor 3 alterations and response to PD-1/PD-L1 blockade in patients with metastatic urothelial cancer. Eur Urol 2019 July 1 (Epub ahead of print).