We read with interest the study by Marri and colleagues (1) suggesting that in patients with classical Hodgkin lymphoma (cHL), the pretreatment cytokine profile, particularly serum levels of IL6 and IL2R, may be used to identify those at high risk for early-disease relapse. The authors further suggest that targeting the cross-talk between Hodgkin–Reed/Sternberg cells and reactive stromal cells in the tumor microenvironment may yield new effective treatment options. Inflammation and angiogenesis are central to the stromal response in solid tumors and lymphomas, and Angiopoietin-2 (Ang-2) is a vascular destabilizing factor that is expressed by endothelial cells at sites of inflammation and vascular remodeling (2). Indeed, a strong prognostic role for pretherapeutic plasma Ang-2 levels has been demonstrated in hepatocellular carcinoma (HCC) (3) and other solid tumors as well as in hematological malignancies (4). To explore the role of Ang-2 in cHL, we took advantage of a cohort of patients with advanced-stage cHL from the HD18 trial (NCT00515554) of the German Hodgkin study group (n = 93), treated with either six or eight cycles of BEACOPP escalated (bleomycin, procarbazine, and prednisone), depending on early tumor response assessed by PET-based interim staging after two cycles of chemotherapy (PET-2).

In line with data from the Framingham cohort (5) of young adults, plasma Ang-2 levels were significantly higher in females than in males in both patients with cHL and age-matched controls (n = 57). Accordingly, Ang-2 levels were compared independently in male and female patients with cHL with age-matched healthy controls. Our analyses demonstrate for the first time that Ang-2 levels are significantly elevated in advanced-stage cHL: Female patients (n = 50) versus healthy controls (n = 36): 8596.6 ± 8970.4 pg/mL versus 3676.4 ± 1434.1 pg/mL; P < 0.0001; male patients (n = 43) versus healthy controls (n = 29): 3198.2 ± 1757.5 pg/mL versus 2208.3 ± 781.4 pg/mL; P < 0.0239. Regarding the international prognostic score, there was no correlation in female patients with cHL (P = 0.4) and a weak correlation in male patients with cHL (P = 0.0267). In this cohort, PET-2–negative and PET-2–positive patients were evenly distributed, and no significant correlation with early PET response, which represents a strong prognostic marker, was found in both male and female patients. Taken together, our findings complement the data by Marri and colleagues (1) indicating that Ang-2 is involved in the stromal response in cHL, although lacking a prognostic value. However, given that Ang-2–targeting compounds are reaching late clinical development for cancer therapy, a potential therapeutic role in cHL should be further investigated.

Disclosure of Potential Conflicts of Interest
No potential conflicts of interest were disclosed.

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Prognostic Serum Cytokines in Classical Hodgkin Lymphoma—Letter

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