suitable for triplet chemotherapy. Currently, there is no evidence to support the perioperative use of any biologically targeted drug, including trastuzumab or any antiangiogenic compounds.

https://www.esmo.org/Guidelines/Gastrointestinal-Cancers/Gastric-Cancer/eUpdate-Gastric-Cancer-Treatment-Recommendations

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Maintenance lenalidomide in primary CNS lymphoma

We read with great interest the promising results of the recent 'proof of concept' phase II study of combination lenalidomide plus rituximab in relapsed primary CNS lymphoma patients from the French Oculo-Cerebral Lymphoma (LOC) Network and the Lymphoma Study Association (LYSA) [1].

We congratulate the investigators for their demonstration of an encouraging median progression-free survival of 7.8 months in this difficult brain tumor population. These results are similar to our own phase I study results in which we demonstrated activity of lenalidomide as monotherapy and in combination with rituximab, yielding a median progression-free survival of 6 months in relapsed, refractory primary and secondary CNS lymphoma patients [2].

However, in comparing their results with maintenance lenalidomide with our own published retrospective cohort of patients that received maintenance lenalidomide, Soussain et al. omitted the fact that the 10-patient cohort of relapsed, refractory primary

CNS lymphoma in our study were managed according to a different protocol, in which they received maintenance low-dose lenalidomide after response to genotoxic therapy (either repeat administration of high-dose methotrexate plus rituximab or focal irradiation). As stated in our report, these patients received maintenance lenalidomide, a targeted agent with immunotherapeutic properties, in the setting of minimal residual disease after remission induction therapy, using agents that have a different mechanism of action. Importantly, the median response duration in complete responses 2 through 5 (after one to four previous relapses) with lenalidomide maintenance was greater than six times longer than response duration after complete response 1 with standard induction therapies ($P < 0.008$) [2]. This is an important contrast to highlight between our study and the phase II study by Soussain et al. in that they evaluated the efficacy of lenalidomide maintenance in relapsed primary CNS lymphoma after up-front lenalidomide and rituximab.

The clinical utility of the strategy of low-dose maintenance lenalidomide after response to genotoxic therapy is further supported by our recent report of low-dose lenalidomide maintenance after methotrexate-based induction therapy in older patients (age 70–86 years) with newly diagnosed primary CNS lymphoma, in which median progression-free survival has not yet been reached after a median follow-up of >35 months [3]. These encouraging preliminary results of prolonged PFS and OS with lenalidomide as maintenance in older patients markedly exceed results of previous prospective clinical trials and population-based studies in elderly PCNSL, in which, at best, the majority of patients exhibit tumor progression within the first year and die within 2 years [4, 5]. It is important to point out as well that Thieblemont et al. [6] recently demonstrated the efficacy of maintenance lenalidomide after complete or partial response to first-line genotoxic therapy with R-CHOP in elderly patients with systemic diffuse large B-cell lymphoma.

Taken together, given that Soussain et al. commented on and compared our findings, it is necessary to clarify that our protocol using lenalidomide maintenance after response to genotoxic therapy is clearly distinct from the definition of lenalidomide maintenance used within the context of their phase II trial. While our preliminary results of course require prospective validation, we hope that our data are considered accurately by clinicians, particularly given that it may provide an effective therapeutic strategy that prolongs response duration and survival in patients with high-risk and/or refractory primary CNS lymphoma.

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Disclosure

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Reply to the letter to the editor 'Maintenance lenalidomide in primary CNS lymphoma' by Rubenstein et al.

We thank Rubenstein et al. [1] for their interest in our work [2]. The issue being the discrepancy of the effect of a similar maintenance treatment with lenalidomide between their retrospective series of 13 elderly patients [3] and our prospective REVRI trial evaluating the combination of Rituximab and lenalidomide in relapse/refractory primary CNS lymphoma (PCNSL) and followed in responder patients by a maintenance treatment with lenalidomide alone. First of all, in the discussion of our article, we mentioned the results of the lenalidomide maintenance of the study by Rubenstein et al. [4] obtained from a retrospective series of 10 patients without discrediting them and stated that the results of the maintenance phase in our study were disappointing compared with their results. At the time of the submission of the REVRI study, the letter by Vu et al. [3] reporting encouraging results of low dose (5 mg/day) of lenalidomide from a retrospective series of 13 patients was not published yet.

We fully agree with Rubenstein et al. that lenalidomide in maintenance was not given in the same situation in these two