Reviewer's report

Title: Assessment of the consistency and robustness of results from a multicenter trial of remission maintenance therapy for acute myeloid leukemia

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Reviewer: Thomas Büchner

Reviewer's report:

This manuscript deals with a previous publication on the effect of HDC/IL-2 as maintenance treatment in AML. This paper had been shown a significant prolongation of LFS but not of OS. The authors now analyzed the consistency and robustness of the effect on LFS. Therefore LFS with hazard ratios was investigated in forest plots according to risk groups and countries to test for consistency whereas robustness was tested using “leave-one-center-out” analyses. Both methods resulted in clear evidences for a consistent and robust prolongation of LFS by HDC/IL-2 also supporting the conclusion that LFS can serve as a surrogate parameter for OS. The authors even recommend a restriction to the surrogate parameter LFS in similar clinical trials where the number of patients does not power for effects on OS.

Major compulsory revisions:

While the statistical calculations appear convincing their correctness should be judged about by a statistical expert.

Since remission duration and relapse are sensitive endpoints, the exact plan and method of monitoring remission and relapse should be given. A systematic difference in this regard between the randomized groups should be excluded. The number of allogeneic transplantations in 1st remission in both randomized groups should be given. LFS also covers NRM possibly due to allogeneic transplantation. M3 AML should not be included.

Further comments:

1. The question posed is new and well defined.
2. The methods are appropriate and well described.
3. The data are sound.
4. The manuscript adheres to relevant reporting standards.
5. The discussion and conclusions are well supported by data.
6. Title and abstract are accurate.
7. The writing is very good.

Level of interest: An article of outstanding merit and interest in its field

Statistical review: Yes, but I do not feel adequately qualified to assess the
statistics.

Declaration of competing interests:

The reviewer received reimbursements and honoraria at the occasion of advisory board sessions from Epicept Corporation