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# LB2711 BMT-CTN 1506 (MORPHO): A RANDOMIZED TRIAL OF THE FLT3 INHIBITOR GILTERITINIB AS POST-TRANSPLANT MAINTENANCE FOR FLT3-ITD AML

**Topic:** Late-Breaking Oral Session

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**Background:**

Patients with acute myeloid leukemia with an internal tandem duplication mutation of FLT3 (FLT3-ITD AML) have a high risk of relapse and routinely undergo allogeneic hematopoietic cell transplantation (HCT). FLT3 inhibitors are often administered as post-HCT maintenance therapy to decrease relapse risk, but this practice is based on randomized studies of sorafenib that included patients salvaged with FLT3 inhibitors pre-transplant.

**Aims:**

BMT-CTN1506 ("MORPHO") was an international phase 3 randomized placebo-controlled, double blinded study of post-HCT maintenance with the FLT3 inhibitor gilteritinib. The primary objective was to determine if post-HCT maintenance with gilteritinib improved relapse-free survival (RFS) compared with placebo for participants (pts) with FLT3-ITD AML transplanted in first remission. Overall survival (OS) was a key secondary objective. Additional secondary objectives included examining the effect of measurable residual disease (MRD) pre- and post-transplant on RFS and OS, rates of non-relapse mortality, event-free survival, and acute and chronic graft-versus-host disease (GVHD) in participants treated with gilteritinib versus placebo.

**Methods:**

Adults with FLT3-ITD AML in first remission after receiving no more than two cycles of induction therapy with HCT planned within 12 months of achieving remission were screened for eligibility. After induction and any

consolidation therapy, pts were registered and underwent HCT. After engraftment, between 30-90 days after HCT, they were randomized to placebo or 120 mg/day gilteritinib for 24 months. Marrow aspirates for MRD were collected pre-transplant, pre-randomization, and at 3, 6, 12, 18, and 24 months post-randomization. MRD was analyzed using a PCR-NGS assay that could detect a FLT3-ITD mutation at a level of 1 x $10^{-6}$. Randomization was stratified by pre-HCT MRD of $10^{-4}$ or greater, conditioning regimen intensity, and time from HCT to randomization of -/+ 60 days.

**Results:**

We screened 620, registered 488, and randomized 356 pts. By intention-to-treat analysis, RFS (Figure 1A) was higher for pts randomized to gilteritinib, but the difference was not statistically significant (HR: 0.679; 95% CI: 0.459, 1.005; 2-sided p-value: 0.0518). OS was similar in both groups (HR: 0.846; 95% CI: 0.554, 1.293; 2-sided p-value: 0.4394 (Figure 1B). Two-year RFS was 77.2% (95% CI 70.1%, 82.8%) for gilteritinib and 69.9% (95% CI: 62.4%, 76.2%) for placebo. 50.6% of pts had MRD ($10^{-6}$ or greater) pre-HCT or pre-randomization. In pre-specified subgroup analysis, the effect of gilteritinib was more pronounced in pts with detectable MRD (HR=0.515, 95% CI: 0.316, 0.838, p = 0.0065) than in pts without detectable MRD (HR=1.213, 95% CI: 0.616, 2.387, p = 0.575) (Figure 2). 143 (80.3%) in gilteritinib arm and 129 (72.9%) in placebo arm experienced dose interruptions and 97 (54.5%) in gilteritinib arm and 45 (25.4%) in placebo arm required dose reductions. Treatment-emergent adverse events (TEAE), including neutrophil decrease (42.1 versus 15.8%) and chronic GVHD (52.2 versus 42.1%), were more common in the gilteritinib arm, as were TEAEs leading to withdrawal of treatment.

**Summary/Conclusion:**

Gilteritinib appears to have a clear benefit for the 50% of pts with detectable MRD pre- or post-HCT, compared to those without detectable MRD. TEAEs associated with gilteritinib were primarily myelosuppression and increased incidence of chronic GVHD. These data are among the first to support the effectiveness of MRD-based post-HCT maintenance therapy.

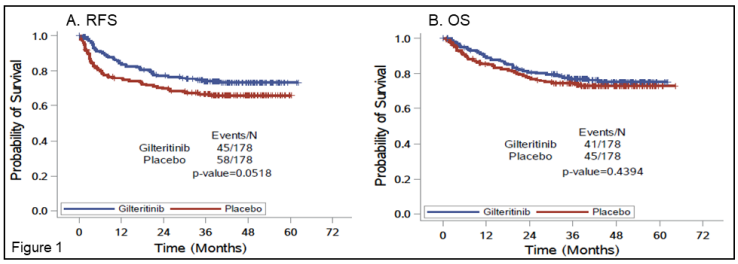

Figure 1

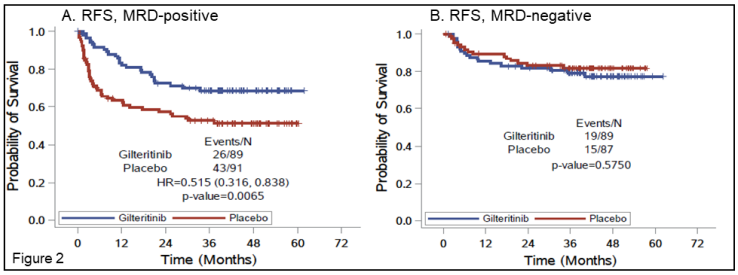

Figure 2