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Second interim analysis of a phase 3 study of idelalisib plus rituximab (R) for relapsed chronic lymphocytic leukaemia (CLL): efficacy analysis in patient subpopulations with Del(17p) and other adverse prognostic factors

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Idelalisib, an oral inhibitor of PI3Kδ, was recently approved for the treatment of relapsed CLL in combination with rituximab (IDELA+R). This report describes results from the second interim analysis of the Phase 3 study evaluating IDELA+R.

The study evaluated IDELA+R versus placebo (PBO)+R in patients with CLL requiring therapy after progression <24 months since last therapy and considered unfit to receive cytotoxic therapy. Patients were randomised to receive IDELA (n = 110) or PBO (n = 110) in combination with R. After progression, patients could enrol into a blinded extension study. Median age was 71 years (78% ≥65 years) with a median number of 3 prior therapies (range: 1–12). 43% had deletion (17p)/TP53 mutation, and 84% had unmutated IGHV. At the time point of the data cut-off for this analysis the median (range) exposure was 5 (0–17) months on IDELA+R and 4 (0–15) months on PBO+R. 76% of patients on IDELA+R and 46% of patients on PBO+R were continuing on study. Median PFS was not reached for patients on IDELA+R and was 5.5 months for patients on the comparator arm. ORR was 77% in the IDELA+R group and 15% in the PBO+R group. Median OS was not yet reached.

Adverse events (any Gr/Gr ≥3) occurring in ≥20% of patients on IDELA treatment were: pyrexia (IDELA+R 35%/3%; PBO+R 17%/1%), fatigue (IDELA+R 28%/3%; PBO+R 27%/2%), nausea (IDELA+R 26%/0%; PBO+R 21%/0%), chills (IDELA+R 21%/2%; PBO+R 16%/0%), diarrhoea/colitis (IDELA+R 21%/5%; PBO+R 15%/0%). ALT/AST elevation (any Gr/Gr ≥3) occurred in 40%/8% of patients on IDELA+R and in 20%/1% of patients on PBO+R. At the time point of this analysis, 19 total deaths had occurred on the primary study, 6 on IDELA+R and 13 on PBO+R.

IDELA+R demonstrated statistically significant improvement over PBO+R in PFS, ORR, and OS with an acceptable safety profile in these frail relapsed CLL patients.

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Updated efficacy including subgroup analyses and safety in the phase 3 RESONATE™ trial of ibrutinib versus ofatumumab in previously treated chronic lymphocytic leukaemia/small lymphocytic lymphoma

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Ibrutinib (Imbruvica™), a first-in-class Bruton's tyrosine kinase inhibitor, is a once-daily single agent approved by EMA for CLL patients with ≥1 prior therapy or with 17p-deletion or TP53-mutated CLL. We report updated results for the phase 3 RESONATE™ (PCYC-1112) study of ibrutinib versus ofatumumab.

Patients received 420 mg oral ibrutinib daily until progression or unacceptable toxicity, or IV ofatumumab for ≤24 weeks. Primary endpoint: IRC-assessed PFS. At interim analysis (median 9.4-month follow-up) the Independent Data Monitoring Committee recom-