Health-related quality of life (HRQoL) is an important element when considering treatment selection, especially related to treatment toxicity. As no new drugs had been approved for AML in the United States in over 4 decades (Bose 2017), idosidenib is a once-daily, oral therapy in clinical trials for the treatment of IDH1-mutated (mIDH1) R/R AML. The phase 1, single-arm trial showed a complete remission or remission with partial hematologic recovery rate of 30.4% and a 30% of patients surviving 5 years from their diagnosis (National Cancer Institute 2012 for comparators the relative QALYs gained with ivosidenib increased, driven by gains in LYs).

**METHODS**

- **Model Methods**
  - A partitioned survival model over a lifetime (5-years, less than 1% of the population alive) time horizon with 1 week cycles, leveraging event-free survival (EFS) and overall survival (OS) curves considered the impact of clinical performance and AEs on HRQoL. Three health states were considered in the model: EFS, progressed disease (PD) and death. The model estimated total life years (LYs) and quality-adjusted life years (QALYs). Health state utilities are used to calculate QALYs, where 1 equals perfect health and 0 equals death. The total number of LYs is adjusted by the health state utilities to calculate QALYs (Whithead 2010).
  - **Comparators**
    - The model was developed for the mIDH1 R/R AML population (Agios data on file). Comparators were therapies that are used to treat R/R AML, as informed by a review of treatment guidelines and discussions with practicing oncologists.
  - **Survival**
    - Given the heterogenous data for the model comparators, two survival approaches were taken in the model.
      - Using published survival data for the phase 1 idosidenib trial for all interventions (Agios data on file) which only considers a difference in the AE profiles of the comparators relative to idosidenib.
      - Using published survival data from a phase 3 R/R AML clinical trial of cytarabine + velaritabine for all comparators (Faderl 2012) which considers differences in both AE profiles and survival relative to idosidenib.
  - **Clinical inputs**
    - Duration of therapy and number of cycles
    - Interventions requiring induction and consolidation were assumed to have two cycles of treatment. Low dose cytarabine (LoDAC) and hypomethylating agents (HMAs) were administered for two and four cycles, respectively. Induction was assumed to be administered over the course of the EF5 health state.
    - Time to remission
    - Time to remission for idosidenib was 12.17 weeks based on the phase 1 data (Agios data on file). For the remaining therapies, remission was assumed to be achieved upon completion of treatment.
  - **Health State Utilities**
    - Given a lack of published information on baseline HRQoL, (without treatment-based adjustments) in the R/R AML population, health state utilities were derived from the published literature based on a first-line AML population (Table 1).

**RESULTS**

- **Base Case Results**
  - Assuming idosidenib survival is identical to comparators (e.g., relative survival benefits assumed), ivosidenib produces slightly more QALYs versus comparators, while using the survival data from Faderl for 2012, the comparator survival models gained with ivosidenib increased, driven gains in LYs.
  - Given the lack of head-to-head data in the phase 1 ivosidenib trial and the limited number of published studies in the R/R AML population with both EFS and OS data, the Faderl 2012 study was used as a proxy. This data may not be representative of the population studied in the phase 1 ivosidenib trial, as it was based on patients who had received s2 prior regimens (Faderl 2012) and thus would be expected to demonstrate better efficacy chemotherapy and OS than patients in the ivosidenib trial who had received a median of 2 prior regimens.
  - There are several additional limitations to note in this analysis:
    - Health state utilities were from the first-line AML population and AE disutilities were derived from the broader oncology literature base.
    - However, scenario analysis varying these values produced the same trends as seen in the base case analysis.
  - Patient management in R/R AML is dependent on response to treatment. This analysis simplified the pathway and assumed a consistent duration of treatment for model comparators (2 induction/consolidation cycles, median number of cycles for other therapies).

**CONCLUSIONS**

- **Given the potential for improved survival and its favorable AE profile versus other R/R AML therapies, idosidenib is expected to improve HRQoL over patients’ lifetime in the mIDH1 R/R AML population.**
- **When varying the AE disutility, as well as health state utilities and AE utility, the results consistently showed that ivosidenib produces greater QALYs versus other R/R AML comparators.**
- **A key area for future research is to gather more detailed information on baseline HRQoL in the R/R AML population and use follow-up data, where possible, on patient outcomes and health state utilities to better understand patient outcomes for mIDH1 patients on new treatments, such as idosidenib.

## References