A Model-based Assessment of the Benefits and Risks of Ponatinib versus Bosutinib in Third-line Treatment of Chronic-Phase Chronic Myeloid Leukemia (CP-CML)

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BACKGROUND

- Ponatinib is a potent and tyrosine kinase inhibitor (TKI) that is active against unmutated and mutated BCR-ABL, discontinued, or CML, including the T315I mutation.
- Ponatinib and bosutinib are TKIs commonly used after failure of 2 or prior TKIs, consistent with their approved indications.
- Estimated probabilities of achieving complete cytogenetic response (CCyR) as well as major cytogenetic response (MCyR) among patients on CP-CML were substantially higher for ponatinib than for other 2nd-generation (2G) TKIs, when compared individually.
- The Phase III (PACE) study evaluating ponatinib in 3rd-generation (3G) TKIs, as well as the Phase III (Bos-209) study evaluating bosutinib in 3G TKIs, were used to determine the baseline risk of patients being treated with ponatinib or bosutinib.
- Evaluating the clinical significance of differences in CCyR risk between treatments, taking into account risks associated with alternative treatments.

OBJECTIVES

- To quantify the benefits and risks associated with choosing ponatinib versus bosutinib as 3G CML patients who have failed 2 TKIs.

METHODOLOGY

Model Overview

- Model structure: Adult CP-CML patients who have previously failed 2 TKIs.
- Model comparator: ponatinib and bosutinib.
- The model compared benefits and risks of patients from 1 common model that accumulated lifetime 3G TKI utility using QALYs.
- Utilities reflect subjective preferences for different health states.
- Utilities are measured on an interval scale with 0 reflecting death and 1 reflecting perfect health.
- Utilities are applied proportionately in the response health state.
- Patients born with survival risks and aged proportionately across individuals to generate 3G TKI survival.
- Model outcomes: QALYs and life years.
- Patients are always in one of a finite number of discrete health states.
- Movement between states is dictated by transition probabilities that may change over time.
- The Markov model is used to estimate the time spent in each health state, as well as the survival utility and other outcomes measured over time.

Model Structure

- Markov model: 3 transitions from Figure 1, and 2 transitions from Figure 2.
- The model captures response and non-response to treatment, and includes both treatment- and chronic-adverse event-related utilities.
- Response is defined as achieving CCyR at 12 months.
- Treatment AEs are considered to occur immediately with onset of treatment, prior to entry into the Markov model, and are modeled with utility reduced by 0.7, 1 and 1.2 for severe, moderate, and mild AEs, respectively.
- The Markov model is used to estimate the time spent in each health state, as well as the survival utility and other outcomes measured over time.

Model Inputs

- Model assumptions: AKI (H1) and life years.
- AKI at least grade 3 and chronic AEs (H2).
- Time horizon: 10 years.
- Utilities: Reflects the general population.
- Transition rates: Markov model.
- Definition of time horizon: 10 years.
- Chronic AE: All chronic AEs.
- Utilities: 0.55 for no response, 0.9 for CCyR, 0.8 for major molecular response (MMR) (H3).
- AEs: Time horizon: 10 years.
- Chronic AE: All chronic AEs.
- Utilities: 0.55 for no response, 0.9 for CCyR, 0.8 for MMR.

RESULTS

- Table 3: Scenario Analysis
- Not QALY Difference Between Treatments
- Best Case
- US only patients to 7K, all health states have slightly increased utility vs. US only patients compared with the full study population, baseline disease 97% vs. 98% and dosing 97% vs. 98%.

REFERENCES

- 2. Bosutinib Prescribing Information.