

## Quality-adjusted life years assessment using cabozantinib for patients with advanced hepatocellular carcinoma (aHCC) in the CELESTIAL trial.

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**Background:** In patients previously treated for aHCC, cabozantinib (cabo) led to longer overall survival and progression-free survival vs placebo (pbo) in the randomized, phase 3 CELESTIAL trial (NCT01908426; N = 707). CELESTIAL was stopped early for benefit at the second interim analysis. This *post hoc* analysis estimated the incremental quality-adjusted life years (QALYs) accrued in CELESTIAL.

**Methods:** Health utility was elicited at each study visit using the EQ-5D-5L quality of life questionnaire. (completed by 82–100% of patients overall). UK crosswalk tariffs were applied for health states. Cumulative QALYs by patient were calculated by linear interpolation; for patients who were censored (31% of patients; including 9% within 100 days of randomization), the last observed utility value was carried forward to study end. The difference in restricted mean QALYs was calculated using generalized linear models, accounting for baseline utility, and with 0.06–0.08 QALYs considered the minimal important difference.

**Results:** At day 50 after randomization (acute treatment phase), cabo was associated with a small reduction in mean total QALYs vs pbo (difference  $-0.003$ ; 95% CI  $-0.005$  to  $-0.002$ ;  $p \leq 0.001$ ;  $n = 601$  [cabo,  $n = 389$ ; pbo,  $n = 212$ ]). At day 100, there was a numerical benefit in mean total QALYs for cabo (difference  $+0.007$ ; 95% CI  $-0.001$  to  $0.015$ ;  $p = 0.103$ ;  $n = 627$  [cabo,  $n = 410$ ; pbo,  $n = 217$ ]), and at day 150 the difference was  $+0.032$  QALYs (95% CI  $0.017$  to  $0.047$ ;  $p \leq 0.001$ ;  $n = 629$  [cabo,  $n = 412$ ; pbo,  $n = 217$ ]) in favor of cabo. Over the entire follow-up, patients randomized to cabo accrued a mean of  $+0.092$  (95% CI  $0.016$  to  $0.169$ ;  $p = 0.018$ ;  $n = 700$  [cabo,  $n = 465$ ; pbo,  $n = 235$ ]) additional QALYs compared with those receiving pbo. Using alternative Devlin weights for health states, the mean accrued QALYs with cabo was  $+0.115$  vs pbo (95% CI  $0.032$  to  $0.198$ ;  $p = 0.007$ ).

**Conclusions:** Cabo was associated with an initial, small reduction in health utility. However, with continued treatment, health utility increased and at the end of the study there was a clinically and statistically significant benefit in mean QALYs in favor of cabo.