Letter to the Editor

Clinical Cancer Research

FDA Approval Summary: Sonidegib—Letter

Bishal Gyawali and Yuichi Ando

We read with interest the FDA approval summary for sonidegib, an inhibitor of the Hedgehog signaling pathway and smoothened receptors, for patients with locally advanced basal cell carcinoma (1). On the basis of the results from the randomized BOLT trial (2), sonidegib was approved by the FDA for this indication. This trial tested two different doses of sonidegib: 800 and 200 mg daily. However, because dose–response relationship was observed only for safety but not efficacy (800 mg compared with 200 mg led to increased toxicities without improving efficacy), 200 mg was chosen as the recommended dose for approval. We believe that a few caveats from early-phase trials should be mentioned to allow proper dosing and individualized therapy.

In the early phase I trial of sonidegib carried out in the Western population, the MTD was recommended as 800 mg daily (3). However, in a phase I trial conducted among Asian patients, the recommended dose (RD) was determined at 400 mg daily, only half of the MTD for the Western population (4), suggesting a difference in tolerability between the ethnicities. The randomized phase II BOLT trial leading to FDA approval predominantly included White patients and tested doses of 800 and 200 mg only. Therefore, the current FDA-approved dose of 200 mg might be an overdose for Asian patients and a lower dose, for example, 100 mg, might be more optimal to achieve better risk–benefit ratio of sonidegib for Asian patients. Because the population of United States is heterogeneous, this information is of importance to avoid overdosing and unnecessary toxicities among Asian U.S. patients. For the same reason, we encourage wider enrollment of patients from all races in randomized controlled trials evaluating a novel drug's efficacy and safety.

Disclosure of Potential Conflicts of Interest

Y. Ando is a consultant/advisory board member for Novartis. No potential conflicts of interest were disclosed by the other authors.

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