BACKGROUND

In Switzerland and Australia, sonidegib is also indicated for patients with locally advanced basal cell carcinoma (laBCC). Basal cell carcinoma (BCC) is the most common skin cancer1

OBJECTIVES

- Binding of HH signaling ligand to PTCH1 leads to release of SMO
- Selective inhibition of the SMO protein

METHODS

BOLT Study Design

- BOLT was a randomized, double-blind phase 2 clinical trial conducted in 66 centers across 12 countries
- Adults enrolled had either histologically confirmed laBCC (not necessarily operable due to surgery or radiation) or had mBCC (where all other treatment options had been exhausted)
- Patients received either 200 mg or 800 mg of sonidegib once daily (Figure 2)

RESULTS

Patient Demographics and Disposition

- Two-hundred-thirty patients with laBCC (n=194) or mBCC (n=39) were enrolled between July 20, 2010, and January 10, 2013 (Table 1)
- Patients were randomized to sonidegib 200 mg (laBCC, n=46; mBCC, n=13) or 800 mg (laBCC, n=128, mBCC, n=22)3
- Baseline demographics were well balanced between arms

Table 1. Patient Demographics and Disease History

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>laBCC</th>
<th>mBCC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, %</td>
<td>63</td>
<td>61</td>
</tr>
<tr>
<td>Age, years</td>
<td>61</td>
<td>60</td>
</tr>
<tr>
<td>Baseline tumor</td>
<td>81</td>
<td>82</td>
</tr>
<tr>
<td>Arm, mg</td>
<td>200</td>
<td>800</td>
</tr>
<tr>
<td>Prior antineoplastic therapy, %</td>
<td>67</td>
<td>61</td>
</tr>
<tr>
<td>Metastasis, %</td>
<td>52</td>
<td>46</td>
</tr>
<tr>
<td>Nonaggressive subtype for patients with laBCC based on histological/cytological subtype</td>
<td>45%</td>
<td>48%</td>
</tr>
</tbody>
</table>

Safety/Monitoring AEs

- Monitoring of AEs was done according to the National Cancer Institute Common Terminology Criteria for Adverse Events version 4.03
- AEs were assessed by central and investigator review from the first dose until 30 days after the last dose in patients who received at least one dose of sonidegib
- Muscle-related events were also assessed by an independent safety review and adjudication committee composed of three external experts

At the time of the 30-month analysis, >90% of patients in each arm had discontinued treatment4

- AEs leading to treatment discontinuation in the 200-mg arm occurred in 29% of patients compared with 35% in the 800-mg arm
- More patients receiving sonidegib 200 mg QD were able to stay on treatment until disease progression compared to in the 800-mg QD group

Adverse Events Profile for laBCC and mBCC Combined

- At 30 months, the most common (>20%) of patients’ AEs associated with a once-daily 200-mg course of sonidegib were muscle spasms (54%, 51% grades 1-2), alopecia (50%, all grades 1-2), dysgeusia (44%, all grades 1-2), and nausea (39%, 38% grades 1-2)
- Few grade 3-4 AEs were reported
- Increased creatine kinase (CK) and rhabdomyolysis were the most commonly reported serious AEs among all patients
- Because there was no renal impairment, none of the cases of rhabdomyolysis were confirmed

CONCLUSIONS

- At the BOLT 30-month analysis, sonidegib treatment demonstrated long-term safety and tolerability with no new safety concerns emerging in patients with either laBCC or those with mBCC
- Sonidegib 200 mg demonstrated a better benefit-risk profile compared with sonidegib 800 mg QD
- These data support the use of sonidegib 200 mg for the treatment of patients with laBCC or mBCC according to the treatment guidelines

REFERENCES


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