The serine/threonine kinase AKT plays important roles in cellular processes such as cell growth, metabolism, and the regulation of cellular proliferation and survival. AKT is activated in response to various stimuli such as growth factors, insulin, and glucose, and is a key regulator of the mammalian target of rapamycin (mTOR) pathway and the intrinsic metabolic pathway. AKT activation is often found in cancer cells, where it promotes cell growth and survival, leading to resistance to therapy. The drug ARQ 092, a novel oral AKT inhibitor, was evaluated in a Phase 1b study in combination with carboplatin (C) plus paclitaxel (P) in patients with solid tumors to assess its safety, tolerability, and antitumor activity.

**Methods**

Patients were assigned to one of four treatment arms:

- **CP Arm**: Carboplatin 6 mg/mL (AUC 6) and paclitaxel 175 mg/m², Q3W
- **ARQ 092 200 mg BID Arm**: ARQ 092 200 mg BID weekly, carboplatin 6 mg/mL (AUC 6) and paclitaxel 175 mg/m², Q3W
- **ARQ 092 80 mg BID Arm**: ARQ 092 80 mg BID weekly, carboplatin 6 mg/mL (AUC 6) and paclitaxel 175 mg/m², Q3W
- **45 mg C/P Arm**: Carboplatin 45 mg/m², Q3W and paclitaxel 175 mg/m², Q3W

**Drug Administration**

- ARQ 092 was administered orally twice daily on days 1 through 5 of each 21-day cycle of chemotherapy
- Carboplatin and paclitaxel were given every 3 weeks

**Drug Parameters**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Closely Monitored Parameters</th>
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<tbody>
<tr>
<td>ARQ 092</td>
<td>Closely Monitored Parameters</td>
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<tr>
<td>Carboplatin</td>
<td>Closely Monitored Parameters</td>
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<tr>
<td>Paclitaxel</td>
<td>Closely Monitored Parameters</td>
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**Adverse Events**

- The most common (≥ 20%) TEAEs related to ARQ 092 were rash (46%) and fatigue (10%). The most common TEAEs related to C/P were fatigue (91%), neutropenia (64%), anemia (60%), and thrombocytopenia (41%).

**Conclusions**

- ARQ 092 or any chemotherapy.
- Hypokalaemia increased during therapy, and the AUC of ARQ 092 was 6 Q3W.

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