Phase II trial of afatinib in patients with advanced/metastatic urothelial carcinoma with genetic alterations in ERBB receptors 1–3 who failed on platinum-based chemotherapy

**Trial objectives**

To assess the efficacy and safety of afatinib monotherapy in patients with urothelial carcinoma (UC) and ERBB2/ERBB3 amplifications or ERBB2/ERBB3 mutations who have progressed after platinum-based chemotherapy (CT).

**Background**

- Bladder cancer is the commonest cancer of the urinary tract, with ~380,000 new cases and ~150,000 deaths per year worldwide.
- Bladder cancer is the most common cancer of the urinary tract, with ~380,000 new cases and ~150,000 deaths per year worldwide.

**Rationale**

The ERBB pathway is of particular significance for patients with various UC subtypes, which frequently harbour ERBB receptor alterations including ERBB2 amplification, translocation, or amplification, and ERBB3 mutation(s)1,2.

**Study design**

<table>
<thead>
<tr>
<th>Stage</th>
<th>ERBB2/ERBB3 amplification status</th>
<th>Patients with UC+URO given 1st-line treatment of platinum-based IT &amp; metastatic UC (stable or worsening) or ERBB amplification or ERBB3 mutation(s)</th>
<th>ERBB2/ERBB3 amplification status</th>
<th>Patients with UC+URO given 1st-line treatment of platinum-based CT &amp; metastatic UC (stable or worsening) or ERBB amplification or ERBB3 mutation(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 1</td>
<td>ERBB2/ERBB3 amplification status</td>
<td>Patients with UC+URO given 1st-line treatment of platinum-based CT &amp; metastatic UC (stable or worsening) or ERBB amplification or ERBB3 mutation(s)</td>
<td>ERBB2/ERBB3 amplification status</td>
<td>Patients with UC+URO given 1st-line treatment of platinum-based CT &amp; metastatic UC (stable or worsening) or ERBB amplification or ERBB3 mutation(s)</td>
</tr>
<tr>
<td>Stage 2</td>
<td>ERBB2/ERBB3 amplification status</td>
<td>Patients with UC+URO given 1st-line treatment of platinum-based CT &amp; metastatic UC (stable or worsening) or ERBB amplification or ERBB3 mutation(s)</td>
<td>ERBB2/ERBB3 amplification status</td>
<td>Patients with UC+URO given 1st-line treatment of platinum-based CT &amp; metastatic UC (stable or worsening) or ERBB amplification or ERBB3 mutation(s)</td>
</tr>
</tbody>
</table>

**Endpoints and other assessments**

- **Primary**
  - PFS (Cohort A)
  - ORR (Cohort B)
  - Safety

- **Secondary**
  - PFS, OS, OOS, DOR, tumour shrinkage (Cohort A)
  - Safety assessments (including laboratory analyses) will also be performed

**Key findings and conclusions**

- **Objective**
  - To assess the efficacy and safety of afatinib in patients with UC harboring ERBB2/ERBB3 amplifications or ERBB2/ERBB3 mutations who have progressed after platinum-based CT.

- **Study design**
  - Phase II trial using a two-stage design
    - Patients are assigned to Cohort A (ERBB2/ERBB3 amplifications) or Cohort B (ERBB3 amplifications) based on screening biomarkers.

- **Endpoints**
  - Primary endpoints: PFS (Cohort A), ORR (Cohort B)
  - Secondary endpoints: PFS, OS, OOS, DOR, tumour shrinkage (Cohort A)

- **Trial initiation**
  - Trial commenced in June 2016

**References**


**End of text**