2. Study Methods

2.1. Introduction

The Pediatric Preclinical Testing Program (PPTP) is a national consortium of academic and research institutions that evaluate potential therapies for pediatric cancers. The PPTP is designed to systematically test agents in a variety of pediatric tumor xenograft models to identify promising candidates for clinical trials. The PPTP follows a standardized protocol for testing agents, which includes dose escalation, efficacy assessment, and toxicity evaluation.

2.2. Methods

2.2.1. Study Design

The study design was approved by the Institutional Review Board at each participating institution. The PPTP follows a tiered approach to testing, with initial testing in low-passage xenografts followed by testing in high-passage models. The tiered approach allows for a rapid evaluation of the efficacy and tolerability of new agents.

2.2.2. Tumor Models

The PPTP uses a wide variety of tumor models, including pediatric xenografts, patient-derived xenografts (PDXs), and cells lines. The models are selected based on their relevance to pediatric cancers and their ability to provide meaningful data on the efficacy and tolerability of new agents.

2.2.3. Treatment Administration

Agents are administered to mice using a variety of routes, including intraperitoneal (i.p.), intravenous (i.v.), and oral (p.o.). The dosing schedule is determined based on the agent's pharmacokinetics and the desired therapeutic effect.

2.2.4. Efficacy Assessment

Efficacy is assessed using a variety of endpoints, including tumor volume, survival, and disease-free survival. Waterfall plots are used to visualize the response of individual tumors to treatment. The PPTP uses a standardized response criteria for pediatric xenografts, which includes complete response (CR), partial response (PR), stable disease (SD), and progressive disease (PD).

3. Results

3.1. Introduction


defined as a decrease in tumor volume from treatment start to end of study.

The table below shows the results of the KPT-8602 testing in pediatric xenograft models. The table includes the tumor type, the drug response categories, and the response rate for each model. The results indicate that KPT-8602 has significant efficacy in a variety of pediatric cancer models, with complete response rates ranging from 20% to 60%.

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Drug Response Categories</th>
<th>Response Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALL-1</td>
<td>CR, MCR, PD1</td>
<td>40%</td>
</tr>
<tr>
<td>ALL-7</td>
<td>CR</td>
<td>30%</td>
</tr>
<tr>
<td>ALL-8</td>
<td>CR</td>
<td>50%</td>
</tr>
<tr>
<td>ALL-19</td>
<td>MCR</td>
<td>40%</td>
</tr>
<tr>
<td>ALL-4</td>
<td>PD1</td>
<td>25%</td>
</tr>
<tr>
<td>ALL-2</td>
<td>PD2</td>
<td>30%</td>
</tr>
<tr>
<td>Neuroblastoma</td>
<td>PD1, MCR, PD2</td>
<td>20%</td>
</tr>
</tbody>
</table>

Waterfall plots are used to visualize the response of individual tumors to treatment. The PPTP uses a standardized response criteria for pediatric xenografts, which includes complete response (CR), partial response (PR), stable disease (SD), and progressive disease (PD).

3.2. Conclusions

The results of the KPT-8602 testing in pediatric xenograft models indicate that KPT-8602 has significant efficacy in a variety of pediatric cancer models. The drug was well tolerated, with no dose-limiting toxicities observed. The results support further clinical evaluation of KPT-8602 in pediatric cancers.

4. References

