Pediatric Preclinical In Vivo Testing (PIVOT) Data Portal Enables Access to 15 Years of Retrospective Treatment Study Data in Support of Prospective Study Design

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I Introduction

The National Cancer Institute (NCI) established the Pediatric In Vivo Testing (PIVOT) program to collaborate with industry partners to perform preclinical studies to evaluate the potential for targeted cancer agents developed for adults to be applied to pediatric cancers of the central nervous system, leukemia, osteosarcoma, sarcoma, and neuroblastoma.

Cancer Models
Central Nervous System
Leukemia
Osteosarcoma
Sarcoma
Neuroblastoma

PIVOT supports the RACE ACT by providing industry partners access to expertise and infrastructure for evaluating the efficacy of new treatments in pediatric models. The program harmonized 15 years of preclinical data generated by previous preclinical testing programs: the Pediatric Preclinical Testing Program (PPTP) and the Pediatric Preclinical Testing Consortium (PPTC) .

To aid PIVOT investigators with curating, analyzing, and accessing pediatric data, the PIVOT Coordinating Center (U24CA263963) developed the PIVOT Data Portal.

II PIVOT Portal Home Page

When users enter the portal, they are welcomed by a brief description of the PIVOT Portal, summary statistics, and a plot showing the proportional breakdown of agent treatment data for each cancer type. The portal currently contains data for:

- 52 Agents
- 45 Drug Targets
- 34 Drug Classes
- 167 Models

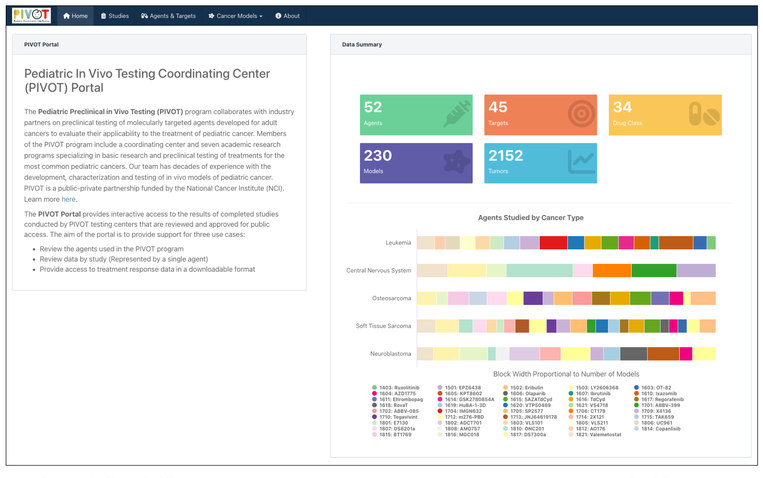

Figure 1: The PIVOT portal home page. Users are greeted with a brief description of the PIVOT program and summary statistics/visualizations of the available datasets.

III PIVOT Portal Features and Organization

The PIVOT Data Portal is a custom R Shiny App that houses preclinical data from consortia members in a centralized location accessible through the Internet. The portal includes features for generating data summaries, statistical reports, tables, visualization of preclinical datasets, and interactively generating study reports.

Treatment study visualizations and data summaries with related metadata can be generated and downloaded within the Shiny App, allowing researchers and computational users to perform further downstream analysis.

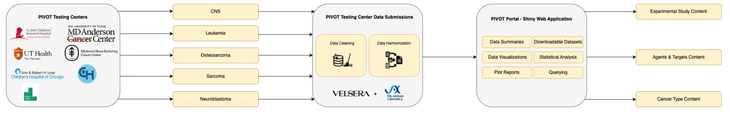

Figure 2: Submitted study data is cleaned and integrated to the PIVOT portal database. The data is used to generate data summaries, visualizations, and statistics; Functionality is grouped by pages focused on either Study, Agents, or Cancer Type

IV Efficacy Studies

The Portal includes study summaries within and across cancer models, statistical reports, tables, and tools for the visualization of treatment results. Data summary tables include entries for Objective Response Measures (ORM), mean outcome, number of tumor studies, and p-values as appropriate. Visualizations include relative tumor volume (RTV) plots (solid tumors), plots of %CD45 (Leukemia), and survival curves (CNS).

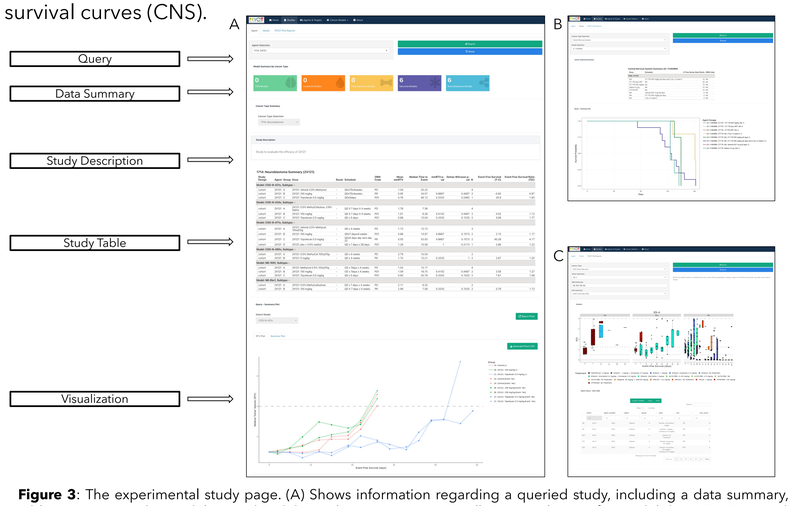

Figure 3: The experimental study page. (A) Shows information regarding a queried study, including a data summary, a table summarizing the models tested and their relevant statistics, as well as a visualization for model data. (B) Data can be queried by model and caner type, which produces a table summarizing the dosing for each model and a corresponding plot. (C) Plot reports can be generated for a particular model and its respective cancer type. The plots compare the event-free survival across different objective response types and time scales.

V Agents

The Portal collectively contains 52 agents, 45 drug targets, 34 drug classes, 167 models, and 2,107 tumors, resulting in a total of 245,926 data points. Currently, 44% of agents have been tested on 2 or more cancer types. The Portal Agent section includes custom visualization. Agent information is easily downloadable into a spreadsheet format.

Figure 4: Overview of available agents and their molecular targets

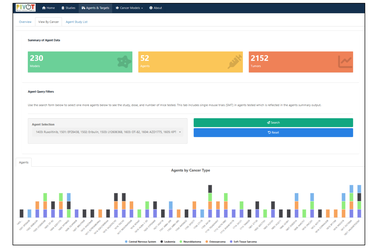

Figure 5: Breakdown of agents by cancer type

VI Pediatric Cancer Types

Figure 6: Users can query data by cancer type and generate a cancers specific type figure

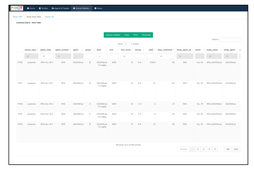

Figure 7: User can view and download data in tabular form.

Contents: The Portal contains data for 5 cancer types accessible. The cancer model types include central nervous system, leukemia, osteosarcoma, sarcoma, and neuroblastoma.

Outcome Description
Among the solid tumor models tested, 10 had at least one treatment that resulted in an ORM of maintained complete response (MCR), while 29 leukemia models had an ORM of MCR.

VII Conclusion

The PIVOT Data Portal supports access to 15 years of retrospective preclinical pediatric cancer study data generated through testing of Patient Derived Xenograft models. Additional study data will be released through the portal in accordance with data release agreements with industry partners. A publicly accessible version of the Portal is planned for 2024.

The Portal provides access to data summaries by study, cancer type, and agent and supports a variety of tabular and graphical options for comparing treatment results within and across studies. Data download is also supported.

We are currently linking the efficacy study data in the portal to multi-omic data generated for the PDX models used in the studies. Merging the existing treatment outcome and genomics data will facilitate computational approaches for studying target identification, personalized treatment, and treatment optimization.

The Pediatric Preclinical In Vivo Testing consortium (PIVOT) provides rigorous preclinical testing of novel molecularly targeted agents using *in vivo* models of pediatric cancer. PIVOT is an extension and expansion of two previous, highly successful NCI programs: Pediatric Preclinical Testing Program (PPTP; 2004-2014) and Pedatric Preclinical Testing Consortium (PPTC; 2015-2021). PIVOT consortium members have decades of experience in developing and using *in vivo* models to advance treatment options for the most common childhood cancers.