Pediatric Early Phase Clinical Trials Network (PEP-CTN)

- Built upon prior experience of COG Phase 1/Pilot Consortium
- PEP-CTN Funded in 2018 after open competition
- Leadership
  - Chair: Brenda Weigel, MD; U of Minnesota
  - Vice-Chair: Elizabeth Fox, MD; SJCRH
  - Statistician: Charles Minard, PhD; Baylor College of medicine
- Utilizes COG clinical trials infrastructure
  - COG Operations Center for protocol development
  - COG Statistics and Data Management center for Medidata Rave study builds and data management
PEP-CTN Member Institutions

- 21 premier COG pediatric core member sites in the U.S.
- 21 non-core member sites in the U.S., Canada and Australia
- Non-core member sites join for phase 2 components of studies and for pilot studies
- Geographic distribution achieved
Clinical Trial Accomplishments

- Completion of **ADVL1412** that defined activity of nivolumab ± ipilimumab for selected pediatric solid tumors

- **ADVL1414** defined RP2D of selinexor that is being used in ACNS1821 study of selinexor + XRT for children with diffuse intrinsic pontine gliomas (DIPG) or other high-grade gliomas

- **PEPN1924** evaluated trastuzumab deruxtecan (DS8201a) in patients with recurrent HER2+ osteosarcoma

- Phase 1 clinical trials of **pevonedistat** with standard of care agents for AML (**ADVL1712**) and for solid tumors (**ADVL1615**)

- Determination of PK behavior for multiple agents
# PEP-CTN Clinical trials

<table>
<thead>
<tr>
<th>Protocol</th>
<th>Phase</th>
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<tbody>
<tr>
<td>PEPN1812 Flotetuzumab in AML</td>
<td>1</td>
</tr>
<tr>
<td>PEPN1924 DS8201a in OS</td>
<td>2</td>
</tr>
<tr>
<td>PEPN2011 Tegavivint in solid tumor incl CNS</td>
<td>1/2</td>
</tr>
<tr>
<td>PEPN21EHR-PBTCN15 EHR Data Transfer Pilot</td>
<td>feasibility</td>
</tr>
<tr>
<td>PEPN2111 CBL0137 in solid tumor incl CNS and lymphoma</td>
<td>1/2</td>
</tr>
<tr>
<td>PEPN2112 Elimusertib in solid tumors</td>
<td>1/2</td>
</tr>
<tr>
<td>PEPN2113 Uproleselan in AML</td>
<td>1</td>
</tr>
<tr>
<td>PEPN2121 Tiragolumab + Atezolizumab in SMARCB1/A4 deficient tumors</td>
<td>2</td>
</tr>
<tr>
<td>PEPN22P1 PK of VCR using BSA banded infant dosing tables</td>
<td>Pilot</td>
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</table>
PEP-CTN and Pediatric CITN (PED-CITN) Clinical Trials

- Support for the CITN will end later in 2023
- Two PED-CITN clinical trials are ongoing in 2023
  - PED-CITN-02: GD2-Targeted Modified T-cells (GD2CART) for Patients with Relapsed/Refractory Osteosarcoma and Neuroblastoma
  - PED-CITN-03: Magrolimab (anti-CD47 MAB) and Dinutuximab in Patients With Relapsed or Refractory Neuroblastoma or Relapsed Osteosarcoma
- The PEP-CTN will assume responsibility for completing PED-CITN-02 and PED-CITN-03
PEP-CTN Clinical Trial Infrastructure Enhancements

- Selected 21 “non-Core” member sites to increase accrual potential for phase 2 trials
- Incorporated central review process for all PEP-CTN clinical trials using the CTSU Source Document Portal
- Adopted DTLs for all PEP-CTN clinical trials and participating in CTEP protocol deviation integration pilot with plans to implement in all future trials
PEP-CTN / PBTC Pilot Study for Electronic Laboratory Data Transfer from Participating Institutions to MediData RAVE

- Develop databases in Medidata Rave on the PEP-CTN and PBTC URLs for sites to directly load lab data from select completed studies from local EHRs
- Map the data extraction process locally and implement tools to enable direct electronic lab data transfer to Rave EDC
- Demonstrate ability to upload lab data to Rave EDC
- Compare lab data received through this process with data entered in Rave EDC during the original conduct of the study
- Assess impact of this process on participating sites and the operations centers of PBTC and PEP-CTN to assess feasibility of utilizing for future studies & expanding implementation consortium-wide
PEP-CTN Accrual and Challenges during Funding Period

<table>
<thead>
<tr>
<th></th>
<th>2018</th>
<th>2019</th>
<th>2020</th>
<th>2021</th>
<th>2022</th>
<th>Grand Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grand Total (Intervention)</td>
<td>95</td>
<td>34</td>
<td>49</td>
<td>44</td>
<td>75</td>
<td>306</td>
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<tr>
<td>Grand Total</td>
<td>95</td>
<td>34</td>
<td>49</td>
<td>95</td>
<td>75</td>
<td>357</td>
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- Year 1 required transitioning procedures and clinical trials from the previous Phase 1/Pilot Consortium to the PEP-CTN and required setting up the Agent Prioritization Committee
- The COVID-19 pandemic during 2020-2022 had impacts both on patient enrollment and on new protocol development
- Enhanced complexity of interactions with pharmaceutical companies resulting from changes in regulatory landscape
- Agents being dropped from clinical development and delays in agents proceeding to clinical development
External Reviewer Feedback (1)

- PEP-CTN identified as an important resource that plays a pivotal role in pediatric drug development
- Streamlining of process for agent prioritization while maintaining high standards for moving agents into pediatric testing
- Need for enhanced communication strategies with pharmaceutical companies
  - More proactive outreach (e.g., regular pipeline meetings)
  - Offering Agent Prioritization Committee feedback to companies on the potential utility of their agents for pediatric cancers
External Reviewer Feedback (2)

- Enhancing interactions with COG Disease Committees to facilitate identification of disease-specific early phase clinical trials that can be performed through the PEP-CTN
- Need for increased engagement with regulatory agencies to ensure that early phase clinical trials developed by PEP-CTN meet both scientific and regulatory purposes
Purpose of RFA

- To support the PEP-CTN to conduct “first in children” studies (i.e., phase 1 often with phase 2 expansion cohorts) as well as phase 2 and pilot studies of promising agents/regimens
  - Molecularly targeted agents
  - IO agents including bispecific T cell engaging agents, CAR T cells, and antibody-drug conjugates
- To define the pharmacokinetic behavior and key pharmacodynamic effects of novel agents in children
- To augment the ability of PEP-CTN to work with pharmaceutical companies by continuing enhancements to its clinical trials infrastructure
Plans for PEP-CTN

▪ Structure:
  ▪ Scientific Leadership
  ▪ Operations and Biostatistics Component
  ▪ Member institutions (Core and non-Core)
  ▪ Pharmacokinetic (PK) and Biology Component
  ▪ Imaging Component

▪ NCI to work with PEP-CTN leadership to enhance capabilities:
  ▪ Streamlining decision-making for agent prioritization
  ▪ Augmenting interactions with pharmaceutical companies, regulatory agencies, & COG Disease Committees to more effectively move agents to testing through PEP-CTN
Budget Considerations

- **Budget for Grant Year 1-5 for current PEP-CTN award:**

<table>
<thead>
<tr>
<th>Year</th>
<th>Approved budget</th>
<th>Less unobligated balance</th>
<th>EHR Supplement</th>
<th>Total federal award amount</th>
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<tbody>
<tr>
<td>2018</td>
<td>$4,739,780</td>
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<td>2022</td>
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<td>$0</td>
<td>$4,153,000</td>
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</table>

- Propose increase of ~ 8% from FY2022 award to $4.5M total cost for Year 1 (FY2024) with a 5-year cost of $22.5M

- Increase justified by higher cost of research activities and by the anticipated conduct of more complex clinical trials that require additional resources to conduct (e.g., CAR T cell studies)
Summary

- PEP-CTN can accelerate the movement of promising novel agents into clinical testing in children
- Important to continue enhancing the capabilities of PEP-CTN for conducting scientifically sound clinical trials that can be used for regulatory purposes
- PEP-CTN plays a central role in NCI’s pediatric cancer research program