Paediatric Drug Optimization (PADO)
Cancer Medicines

GAP•f Global Accelerator for Paediatric formulations WHO Hosted Network

World Health Organization

What is PADO?

PAEDIATRIC DRUG OPTIMIZATION

The development of medicines for children lags unacceptably behind that for adults by nearly a decade. Developing a prioritized drug portfolio of the most needed formulations for children is essential to streamline researchers' and suppliers' efforts and resources around specific dosage forms and formulations that address the most urgent needs for children.

Paediatric drug optimization (PADO) exercises identify key priority products for research and development, led by WHO technical departments and involving relevant stakeholders, and have the potential to accelerate access to optimal formulations in the context of fragmented, small markets for medicines for children.

More information on how to undertake a PADO process and adapt it to the specific needs of each disease area can be found **here**.

BACKGROUND

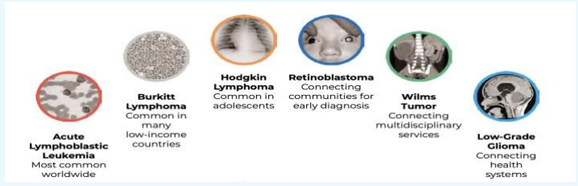
Each year, an estimated 400 000 children and adolescents of 0–19 years old develop cancer. Globally, acute lymphoblastic leukaemia (ALL) is the most common malignancy accounting for an estimated 19% of the total childhood cancer incidence, followed by non-Hodgkin lymphoma, Burkitt lymphoma (5%), Wilms tumour (nephroblastoma) (5%), and retinoblastoma (5%).

There is notable stark gap between the survival rates of 80% in HICs and 20% in LMICs that can be narrowed by decreasing inequities in access to diagnostics, medicines, and innovative mechanisms for overall basic health services – shifts that will impact cancer globally for generations to come. The WHO is collaboratively working with various stakeholders to address these inequities and greatly improve the access gaps in the next decade with this pivotal initiative and platform:

THE GLOBAL INITIATIVE FOR CHILDHOOD CANCER (GICC)

THE GLOBAL PLATFROM FOR ACCESS TO CHILDHOOD CANCER MEDICINES (GPACCM)

The PADO for childhood cancer medicines was designed with the overall goal of better targeting research and development efforts towards those paediatric formulations and medicines that address current needs for GICC target cancers and anticipate future advances in the management of childhood cancers.



KEY OBJECTIVES

1. **Review cancer formulations currently recommended and in use for their appropriateness for paediatric populations**
2. **Identify priority therapeutics to be further investigated and developed for the paediatric population from the EMLc and landscape pipeline analysis**
3. **Develop a clear research agenda to support and enable future drug optimization work meeting the unique needs of the peadiatric cancer population**

PADO Cancer medicines meeting virtually convened on 12th and 17th – 18th January 2024 bringing together key stakeholders to enable alignment among funders, procurers, market- coordination entities, researchers, academics, product development partnerships and regulators involved in priority products to be investigated and developed.

62 *participants from* **21** *countries*

PRIORITY CANCER MEDICINES FOR NEW FORMULATIONS

- CYCLOPHOSPHAMIDE PO
- METHOTREXATE PO/ IT
- ETOPOSIDE PO
- PROCARBAZINE
- MERCAPTOPURINE
- TEMOZOLOMDE

WATCH-LIST CANCER MEDICINES

- RITUXIMAB SQ
- VENETOCLAX

ACCESS CALL OUT FOR CANCER MEDICINES

EXPLORING LICENCSING POSSIBILITIES

- DABRAFENIB
- TRAMETINIB

Global Accelerator for Paediatric formulations GAP•f

a WHO- hosted network, focused on accelerating the process of delivering better medicines to children around the world: **www.gap-f.org**

Click **here** to read the full PADO Cancer medicines meeting report

RESEARCH GAPS TO INFORM DEVELOPMENT

Pharmacokinetic and safety studies

Further research is needed to determine whether rituximab (SC) is better than the IV formulation in terms of efficacy and safety when used in combination with standard chemotherapy regimens for Burkitt lymphoma. This question is raised because of the need to improve access to rituximab in LMICs where availability of IV biosimilars is still limited.

Bioavailability/bioequivalence of venetoclax formulation adapted to children (role in ALL):

- focus on minimizing handling ie. coated granules (toxicity/safety).
- Compare oral suspension formulations to sprinkle/dispersible/minitab preparations.

Diagnostics and stewardship

Development and availability of adequate priority biomarker testing for molecular targeted medicines and immunotherapies suitable for LMIC settings.

Optimizing clinical use

- How to make patented medicines that are approved in HICs accessible in LMICs in a generic form.
- Further investigation to establish role of venetoclax in ALL, AML and neuroblastoma.
- Further investigation on usage of non-liquid oral formulations for temozolomide.
- Explore alternative forms of topotecan for intraocular administration for retinoblastoma.
- Development of a cyclophosphamide + mesna combination formulation.
- Research transit delays and shelf-life of cytotoxic medicines.
- Creation of an optimal formulation of calcium folinate (delivery via patch).
- Studying non-inferiority of oral vs IV formulation for cure protocols and for metronomic or palliative care.
- Will new formulations improve home medication compliance with administering mercaptopurine and methotrexate during the maintenance phase of treatment?

Study design and regulation

- Investigating heat-stable technology (e.g. cold chain or innovative mechanisms for temperature maintenance), and formulations suitable for room temperature that are labelled appropriately.
- Review of toxicity domains (there are many dimensions and considerations that affect practice).

Others

- Expansion of indication for priority formulations to include brain tumours.
- How to make compassionate use available in LMICs.

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