When Less Is More: An Avenue for Academia–Industry Collaboration in Pediatric Cancer

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We read with interest the article by de Wilde et al that explores partnerships between academia and industry in conducting trials for pediatric cancer drug approval.[1] Cancers in the pediatric group have high cure rates and offer the possibility of significant gains in terms of years of life lived in the event of sustained remission. The pace of cancer drug development has traditionally been slower in children, with reported median lag periods of over 5 years for approvals in comparison to adult use.[2] Legislation mandating pediatric studies for drugs being tested in adults has helped accelerate this process over the last decade.[1] However, the global reach of such approvals is limited. Childhood cancer survival rates are reported to be as high as 80% in high-income countries (HICs), while low- and middle-income countries (LMICs) lag behind.[1,3] Treatment abandonment and social barriers to obtaining treatment are significant issues in LMICs, which may be further exacerbated by high costs of care.[4] Thus, drug approval is only an initial step in the process of translating drug development into survival benefits in childhood cancer. The role of academia–pharmaceutical collaborations in enhancing drug access remains unexplored.

Traditionally, the degree of academic involvement in drug trials, as opposed to pharmaceutical company involvement, is higher in pediatric cancers than in adult cancers. The article by de Wilde et al has emphasized the vital role of partnerships between academia and industry in conducting trials for pediatric cancer drug approval.[1] Clinicians can access large hospital databases that provide real-world patient data about drug use patterns, efficacy, and toxicity. They also have more opportunities to understand the patient's perspective holistically regarding reasons for satisfaction with treatment, nonadherence, treatment refusal, and abandonment. Thus, they may be better placed to identify routine clinical problems and design patient-friendly and cost-effective solutions. On the other hand, pharmaceutical companies could provide funding and rigor to trial conduct and may be better equipped to steer trial protocols in a direction that facilitates approval. In India and other LMICs, drug trials are predominantly pharmaceutical driven.[5] The lack of academic involvement in clinical trials may be due to financial, technical, and regulatory constraints. It has been seen that randomized trials of cancer drugs conducted in LMICs are more likely to identify larger effect sizes and identify effective therapies in comparison to those in HICs.[6] Thus, collaborative ventures in LMICs are likely to reap rewards for both academicians and clinicians. ►**Fig. 1** shows how such collaborations may enable better drug access and benefit the partners involved.

Tannock et al found in their review that drug doses used in adult clinical trials of new drugs are often higher than the effective doses identified in earlier phases.[7] Many investigator-initiated trials have explored the efficacy of lower doses of approved drugs (►**Table 1**).[8–12] While some of these trials may have been conducted with the aim of reducing drug-related toxicities with the support of government funding sources, they have the collateral benefit of reducing treatment-related costs and health care resource utilization.[10] In general, cost-reduction strategies are perceived as not being in line with the commercial interests of pharmaceutical companies. However, a few pharmaceutical-funded trials have also attempted to seek out pharmacoeconomic strategies. A pharmaceutical-funded phase III study of low-dose nivolumab in India demonstrated significant improvement in advanced head and neck carcinoma outcomes.[8] This criti-

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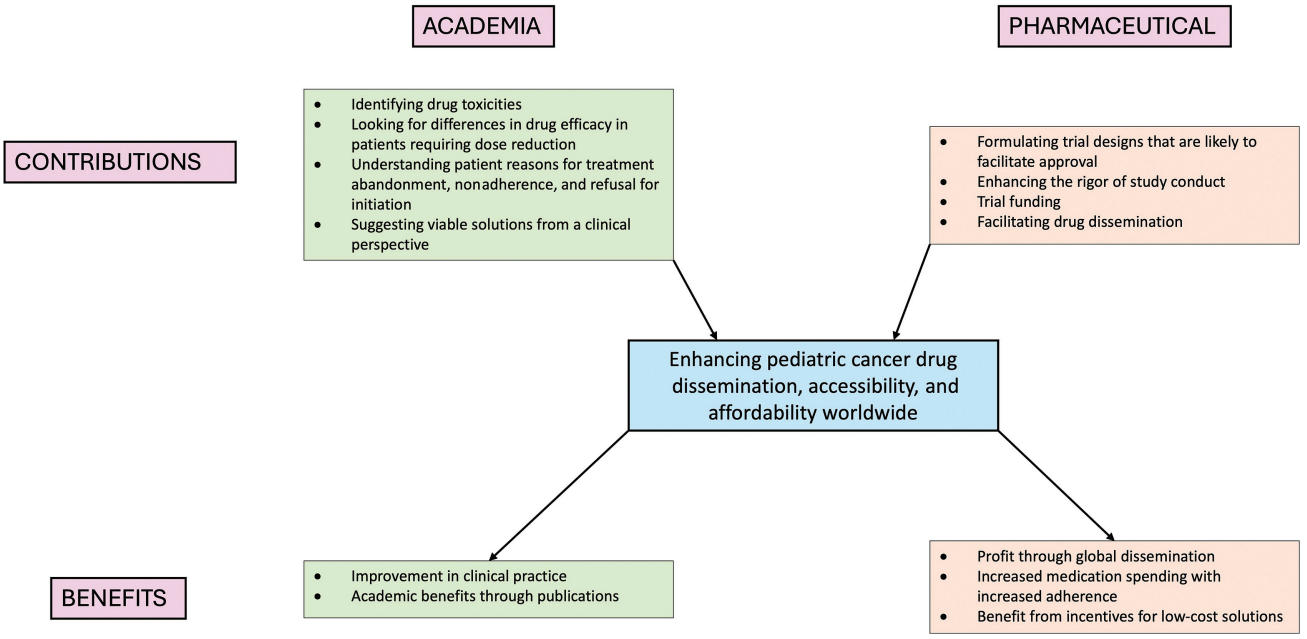

Fig. 1 Academia–drug manufacturer partnerships for enhancing cancer drug access: the contributions of and benefits to each partner.

cal finding has opened up the possibility of expanding the use of immunotherapy for cancer patients in resource-challenged settings.

Cost-effectiveness analyses play a vital role in decision-making for cancer therapeutics. For instance, a retrospective study conducted at a tertiary care center in India showed that oral metronomic therapy and pazopanib showed similar efficacy in the management of advanced soft tissue sarcoma; notably, the cost of oral metronomic therapy was only approximately 1/10th that of pazopanib.[13] However, a systematic review by Al-Badriyeh et al demonstrates that cost-effectiveness analyses sponsored by pharmaceutical companies tend to report results favorable to the sponsor, likely for furthering corporate interests.[14] Pharmaceutical companies could be incentivized by the state to develop innovative low-cost solutions. Drugs found to be cost-effective on independent review may gain the benefit of distribution through the public health care system, thus benefiting both patient care and the pharmaceutical industry.

Although drug manufacturers mention drug development costs as significant contributors to corporate expenditure, drug marketing costs may be greater in magnitude.[15] Drugs that fill a clinician-perceived lacuna in care may potentially have greater uptake among clinicians and patients. Financial toxicity is a significant cause of treatment nonadherence among young cancer patients. Increasing drug adherence

Table 1 Examples of trials exploring the use of lower-dose alternatives for established anticancer drugs in adult cancers

Sl. no.	Drug	Study	Trial description	Funding agency
Targeted therapeutics				
1	Ibrutinib	Chen et al[10]	Pilot study of ibrutinib dose reduction in chronic lymphocytic leukemia	Government
2	Trastuzumab	Earl et al[9]	Phase III trial 6 vs. 12 mo of adjuvant trastuzumab in HER2-positive breast cancer	Government
Immunotherapy				
1	Nivolumab	Patil et al[8]	Phase III randomized study evaluating the addition of low-dose nivolumab to palliative chemotherapy in head and neck carcinoma	Pharmaceutical company
Supportive care drugs				
1	Rasburicase	Vadhan-Raj et al[11]	Trial of single-dose rasburicase vs. daily dosing for 5 d in adult patients at risk of tumor lysis syndrome	Pharmaceutical company
2	Granulocyte colony-stimulating factor	Clemons et al[12]	Trial comparing 5- vs. 7- vs. 10-d schedules of filgrastim for primary prophylaxis of febrile neutropenia in early-stage breast cancer patients	Academic collaboration

could significantly increase medication expenses, thus potentially benefiting pharmaceutical companies. Cost-effectiveness strategies may allow for an increase in drug accessibility to more parts of the world and larger sections of society, which may ultimately allow for monetary benefits through increased consumption. Simultaneously, this may help drastically improve treatment outcomes for childhood cancers in underserved areas worldwide.

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Conflict of Interest
None declared.

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