



Accelerating Anticancer Agent Development and Validation

CDDF-AAADV Satellite Session on Global Pediatric Neuro-Oncology Network AGENDA

Moderators	H. Kim Lyerly/Jaap Verweij	Duke University and CDDF
Pediatric Neuro-Oncology Overview	Roger Packer	Children's National Hospital
Opportunities for improving outcomes in Pediatric Neuro-Oncology in India	Rakesh Jalali	Apollo Hospital
A framework for a Global Pediatric Neuro-Oncology Network: Integrating medical care with clinical research	Kim Lyerly	Duke University
Industry perspective	Chitkala Kalidas	Bayer
Patient perspective	Ruth Hoffman	American Childhood Cancer Organization
Moderated Discussion		
US Regulatory Perspective	Greg Reaman	FDA
EU Regulatory Perspective	Dominik Karres	EMA
India Cancer Center Perspective	CS Parmesh	Tata Memorial Hospital
Closing Remarks and Next Steps	Jaap Verweij	CDDF

Global Incidence

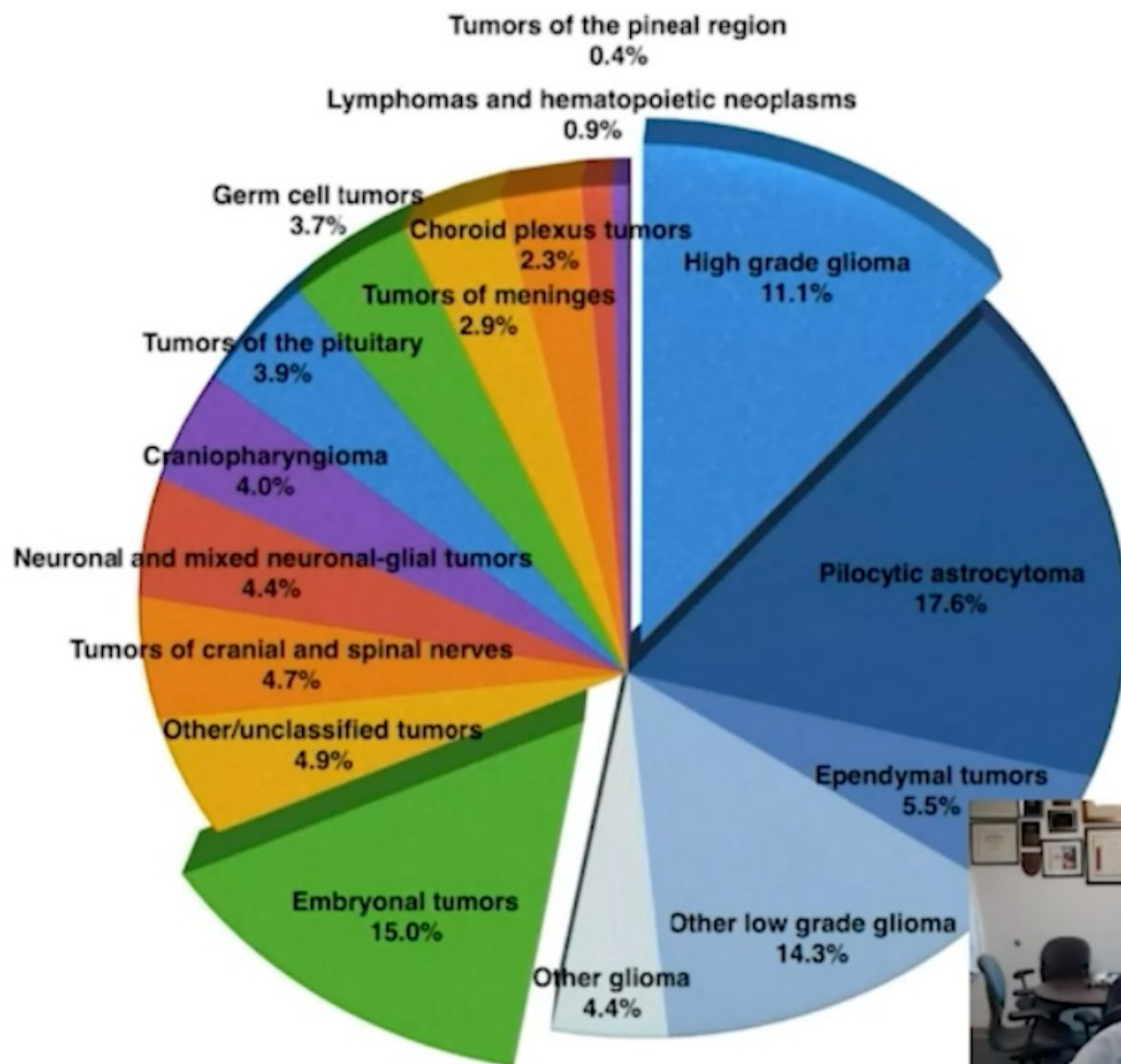


Around the world, more than 400,000 children are estimated to develop cancer every year.

In many parts of the world including the United States, brain tumors are the most common solid tumor found in children, and the **leading cause of cancer-related death** among children ages 0-14 years.

[thelancet.com/journals/lanonc/article/PIIS1470-2045\(20\)30022-X/fulltext](http://thelancet.com/journals/lanonc/article/PIIS1470-2045(20)30022-X/fulltext)

Age 0-14 years (N=16,044)



Pediatric Brain Tumors: Trial Organizations

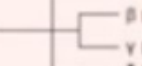
- Children's Oncology Group – NCI funded
 - Largest; USA based – but international
 - Centralized
 - Multiple disease and discipline committees
 - Phase III / Phase II
 - Has Phase I (DVL) component
- Pediatric Brain Tumor Consortium (PBTC) – NCI funded
 - NIH designated “super group”
 - Was USA only until addition of Sick Kids, Toronto
 - Cutting-edge technologies / intricate studies
 - Phase I / Limited Phase II
 - Feeder for Phase II/III to COG
- Department of Defense Neurofibromatosis Clinical Trials Consortium (DODNFCTC)
 - NF1/NF2/Schwannomatosis
- International Society of Pediatric Oncology (SIOP)
 - International
 - Eurocentric, but other international sites (Canada; Australia; South America)
 - Phase II / Phase III
 - Less centralized, countries bring their own funds



Pediatric Brain Tumor: Clinical Trials

- Non-NCI/NIH-funded multi-institutional consortium
 - Pediatric (Pacific) Neuro-Oncology Consortium – PNOC
 - CONNECT
 - Centralized
 - Industry-friendly
 - ? More agile
- Institution led consortium
 - St. Jude's "chosen" consortium
 - Phase I / II / III
 - Disease-type driven
- ReMission
 - University of Florida led
 - Immunologic focus
- Industry run / sponsored trials
 - Increasingly common place
 - Own CRO
 - Focus on FDA labelling
- Multi-site trials
- Single institution trials



Subgroup		WNT		SHH				Group 3			Group 4		
Subtype		WNT α	WNT β	SHH α	SHH β	SHH γ	SHH δ	Group 3a	Group 3 β	Group 3 γ	Group 4a	Group 4 β	Group 4 γ
Subtype proportion													
Subtype relationship													
Clinical data	Age	 	 	 				 	 	 	 	 	 
	Histology			LCA Desmoplastic	Desmoplastic	MBEN Desmoplastic	Desmoplastic						
	Metastases	8.6%	21.4%	20%	33%	8.9%	9.4%	43.4%	20%	39.4%	40%	40.7%	38.7%
	Survival at 5 years	97%	100%	69.8%	67.3%	88%	88.5%	66.2%	55.8%	41.9%	66.8%	75.4%	82.5%
Copy number	Broad	6 ⁺		9q ⁺ , 10q ⁺ , 17p ⁺		Balanced genome		7 ⁺ , 8 ⁺ , 10 ⁺ , 11 ⁺ , 17q		8 ⁺ , 17q	7q ⁺ , 8p ⁺ , 17q	17q	7q ⁺ , 8p ⁺ , 17q (less)
	Focal			MYCN amp, GLI2 amp, YAP1 amp	PTEN loss		10q22 ⁺ , 11q23.3 ⁺		OTX2 gain, DDX31 loss	MYC amp	MYCN amp, CDK6 amp	SNCAIP dup	CDK6 amp
Other events				TP53 mutations			TERT promoter mutations		High GF11/1B expression				

Age (years):  0-3  >3-10  >10-17  >17

Graphical Summary of the 12 Medulloblastoma Subtypes

Schematic representation of key clinical data, copy-number events, and relationship between the subtypes inside each of the groups. The percentages of patients presenting with metastases and the 5-year survival percentages are presented. The age groups are infant <3 years, young child 3-10 years, adolescent >10-17 years, and adult >17 years.



The Good News in the US and High-Income Countries

The five-year relative survival rate for childhood malignant brain tumors is **75.4%**

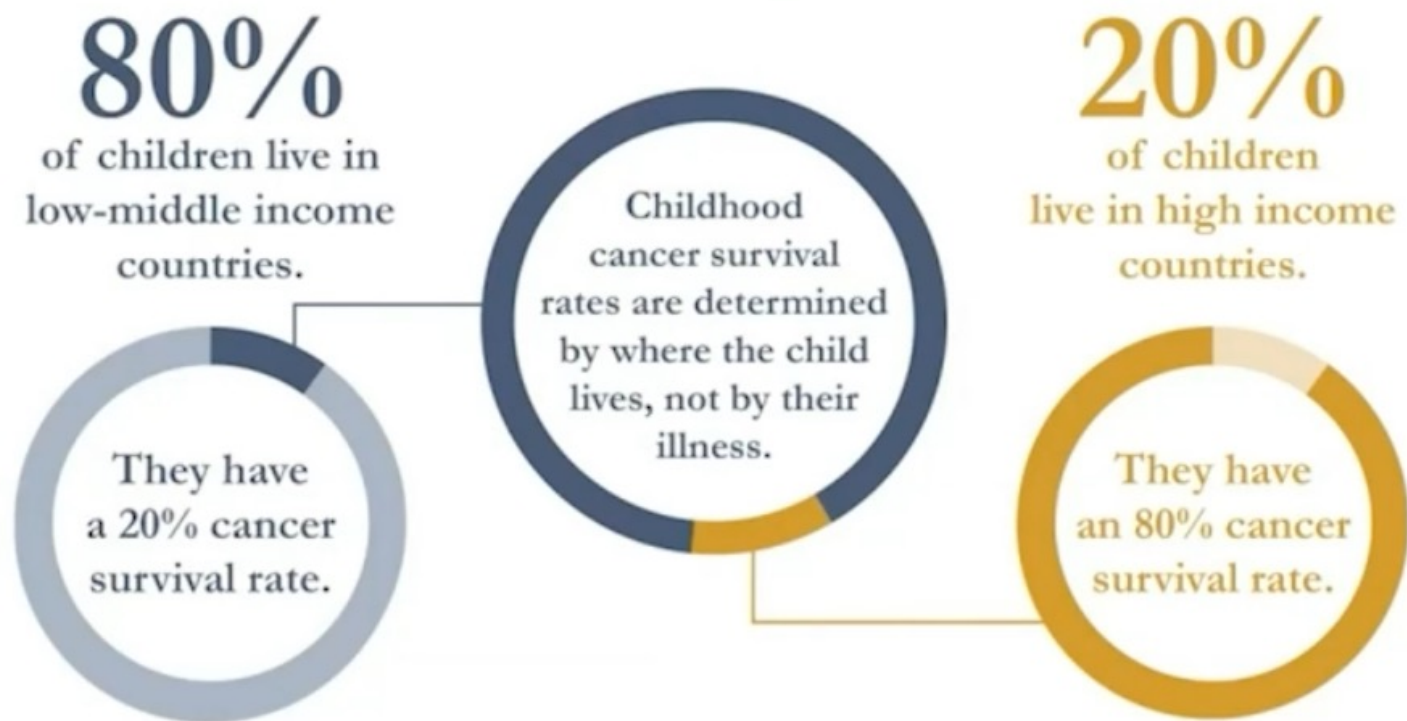
Children have access to comprehensive academic centers, chemotherapy, radiotherapy, surgical expertise, clinical trials, innovative research, family support, NGO and government support.

**AS PARENTS WE
CELEBRATE INNOVATION
& DRUG DEVELOPMENT.**



The Reality for the Rest of the World

Global Disparity



The probability of **survival** for a child with cancer depends greatly on:

- the **socio-economic** background of the **family**
- the underlying health system of the **country** in which they were **born**.

Barriers to Chemotherapy

S. No	Description (Drug name, dosage form, strength and brand)	Retail Unit	Expiry date	QTY at dispensary	QTY at store
1	Atra(All Tra Retinoic Acid)	Tab		247	
2	Bleomycine 15 Unit	Vial		65	20
3	Cisplatine 50mg	Vial		0	
4	carboplatin 450mg/45ml	Vial		0	
5	Cyclophosphamide 500mg	Vial		113	
6	Cytarabine 100mg/ml	Vial		0	
7	Dacarbazine			0	
8	Daunorubicine 20mg	Vial		0	
9	Dactinomycine 0.5mg	Vial		0	
10	Doxorubicine 50mg/25ml	Vial		107	20
11	Ifosfamide 1gm	Vial		50	
12	Etoposide 100mg/ml	Vial		50	0
13	Mercaptopurine 50mg	Tab		1110	
14	Methotrexate 2.5 mg	Tab		400	
15	Methotrexate 50mg/2ml	Vial		124	
16	Vincristine 1mg	Vial		200	20
17	Vinblastine sulphate 10mg/10ml	Vial		40	
18	Dexamethasone 4mg/ml	Amp		0	
19	Dexamethasone 4mg po	Tab		640	
20	Ondansetron 4mg	Tab		40	
21	Ondansetron 8mg	Amp		0	
22	prednisolone			4000	
23	Allopurinol 100mg	Tab		1619.00	
24	L-asparaginase inj 5000IU	Vial		46	
25	mesna			0	
26	Filgrastine(G-CSF)			0	
27	Leucovorin Calcium(folinic acid) 50mg/5ml	Vial		100	



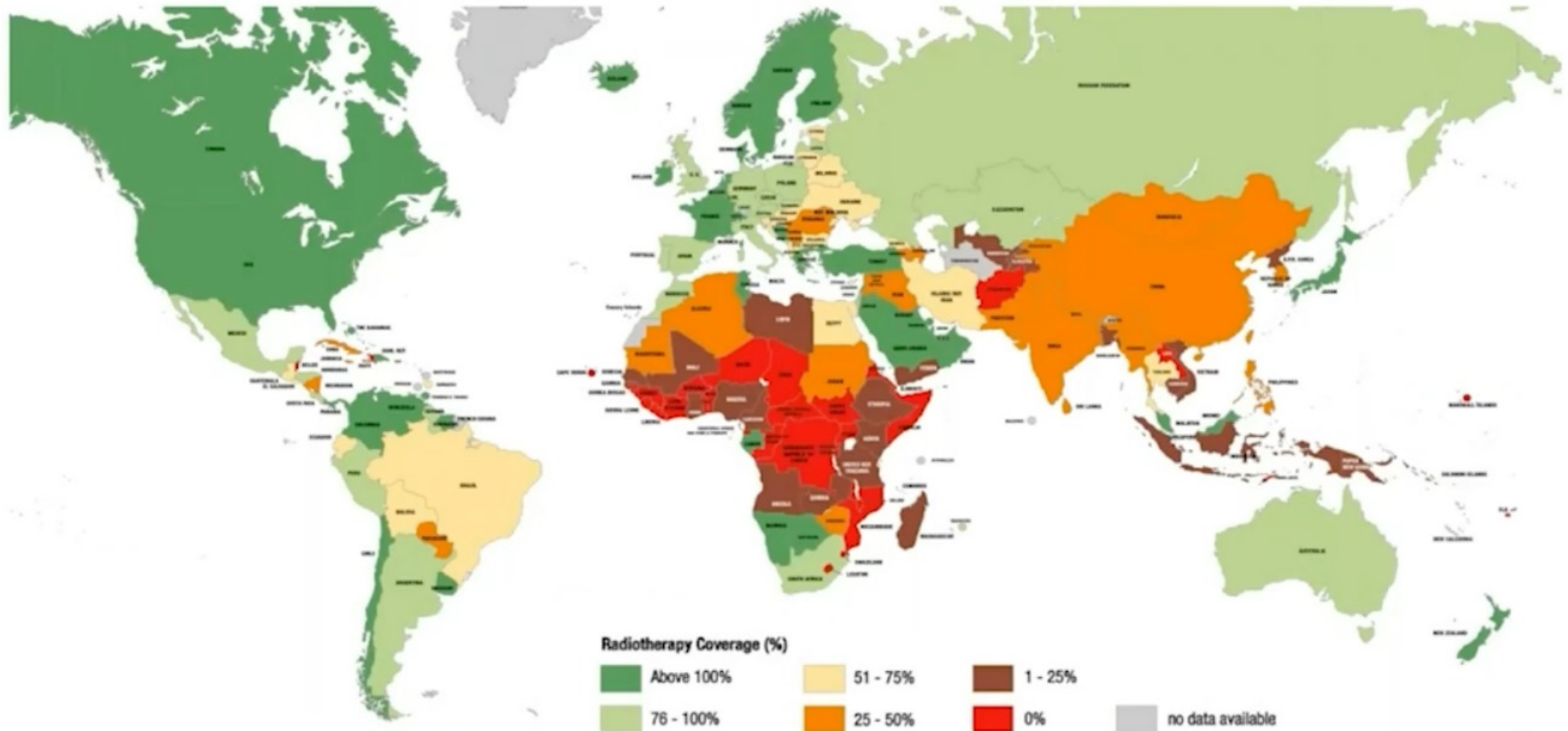
Facilitated collaboration with TEVA and Direct Relief for donation of 17,000 vials of Chemotherapy to Ethiopia.

Research Initiative between Sick Kids, Toronto, Dr. Avram Denburg and American Childhood Cancer Organization (ACCO).

Current: Finishing up 2-year qualitative and quantitative research focused on barriers to chemotherapy in 4 East African Countries (Uganda/1 site, Kenya/4 sites, Tanzania/2 sites, Rwanda/1 site).

Results will be published, utilized by WHO for engagement with MoH regarding possible pooled procurement, policies to reduce barriers.

Inequity in Access to Radiotherapy



Cure All: Global Initiative for Childhood Cancer



The goal of the WHO's Global Initiative for Childhood Cancer (GICC) is to achieve at least a 60% survival rate for all children with cancer by 2030.

This target represents a **doubling** of the current global cure rate for children with cancer, which could result in saving an additional **one million children's lives** in the next decade.

www.who.int/publications/m/item/global-initiative-for-childhood-cancer



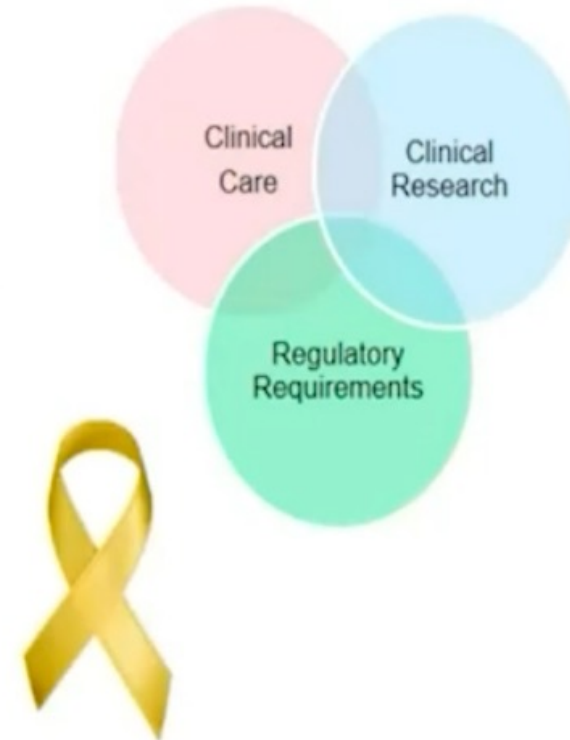
Global Pediatric Neuro-Oncology Network

What can the pharmaceutical industry expect by supporting this network?

A potential sustainable model to address pediatric drug development needs and regulatory requirements

Pre-competitive multi-stakeholder collaborative initiative to support capacity building for treating a vulnerable population with high unmet medical need

Advancement of corporate sustainability goals to reduce disparities in access to quality Cancer Care in underserved populations





A potential sustainable model to address pediatric drug development and regulatory requirements in Neuro-Oncology

Pediatric Clinical Research as a critical component of global Oncology drug development and registration requirements serves to advance development of innovative medicines for children

Although Oncology trials enable early access to innovative therapies, many hurdles exist when it comes to the conduct of pediatric trials¹

- // Ethical challenges
- // Recruitment challenges
- // Infrastructure limitations for pediatric clinical trials

Pediatric Clinical Trial networks provide the opportunity to create a continuum between clinical care and clinical research that can in turn support global pediatric drug development, demonstration of proof-of-concept and also enable registration of drugs



The long-term sustainability of the model depends on processes, organizational structure and partnership among several key stakeholders to create a network that is integrated into the local healthcare system

¹ Lagler FB, et al. 2021



Pre-competitive multi-stakeholder collaborative initiative to support capacity building for treating a vulnerable population with high unmet medical need

Pharmaceutical companies face common challenges when it comes to identifying and recruiting pediatric patients for Oncology trials

- // Recruitment rates are highly variable, but a major rationale for establishing clinical research networks is to complete studies in a manageable time frame
- // Meeting regulatory requirements in terms of number of pediatric patients enrolled in a trial as well as timelines for pediatric commitments are also important considerations

While pediatric clinical trial networks exist in many countries around the world, there is opportunity to extend these networks beyond the traditional footprint to include underserved communities in low and middle income countries (LMIC)

- // This would not only help address some of the challenges pharma companies face with respect to pediatric drug development in Neuro-Oncology but also improve the diversity of the pediatric patient population in clinical trials
- // Local capacity building in the treatment of pediatric brain tumors and the conduct of pediatric clinical trials in low and middle income countries will expand the global clinical trial capacity while at the same time bring much needed access to care in populations with high unmet need





Advancement of corporate sustainability goals to reduce disparities in access to quality Cancer Care in underserved populations

Given the impact of the COVID pandemic, there is an increasing focus on reducing disparities in access to quality health care in underprivileged communities

Bayer's Sustainability strategy is that "Economic Growth and Sustainability Go Hand in Hand"¹

Contributing to the UN Sustainability Development Goal # 3 (Good Health and Well Being) is a key component of Bayer's Sustainability strategy and is aligned with our Corporate Vision of "Health for All"¹

The global pediatric neuro-oncology network is an initiative that can contribute to the goals of pharma companies with a similar sustainability strategy



¹<https://www.bayer.com/en/sustainability/sustainability-strategy>

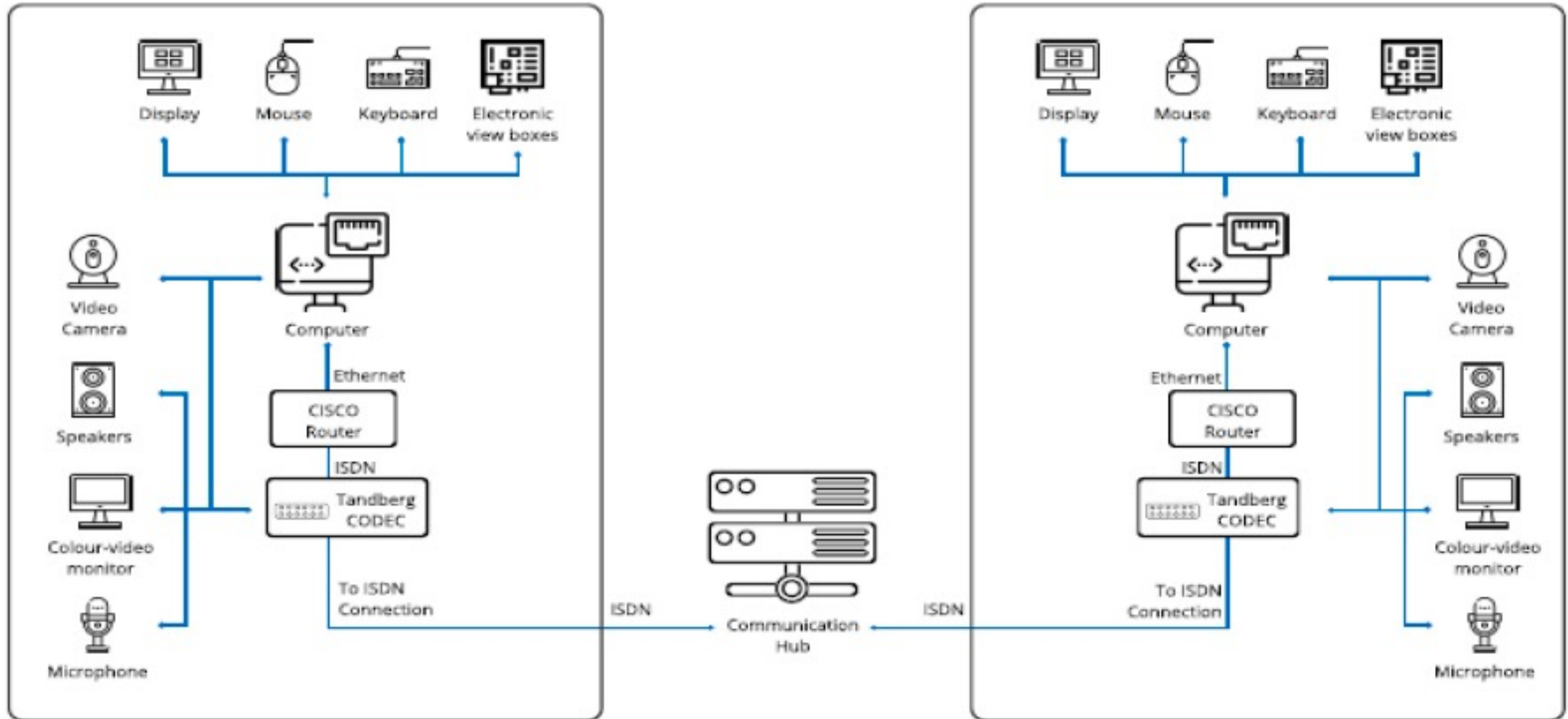
NIH Developed Teleheath Solution: Telesynergy

- First generation Telesynergy software used at NIH-sponsored programs
 - National Cancer Institute (NCI) All Ireland Cancer Consortium
 - NCI Jordan Cancer Collaboration
 - NCI Cancer Disparities Research Partnerships Program

We propose to adopt this open-source software to a cloud-based system with contemporary pathologic and radiologic imaging devices to:

- Enable health practitioners at multiple sites and across geographic borders to simultaneously discuss and view these images

First Generation Telesynergy Platform



First Generation Telesynergy Provided A Same Room Experience



**National Cancer Institute (NCI)
Cancer Disparity Research Project (CDRP)**

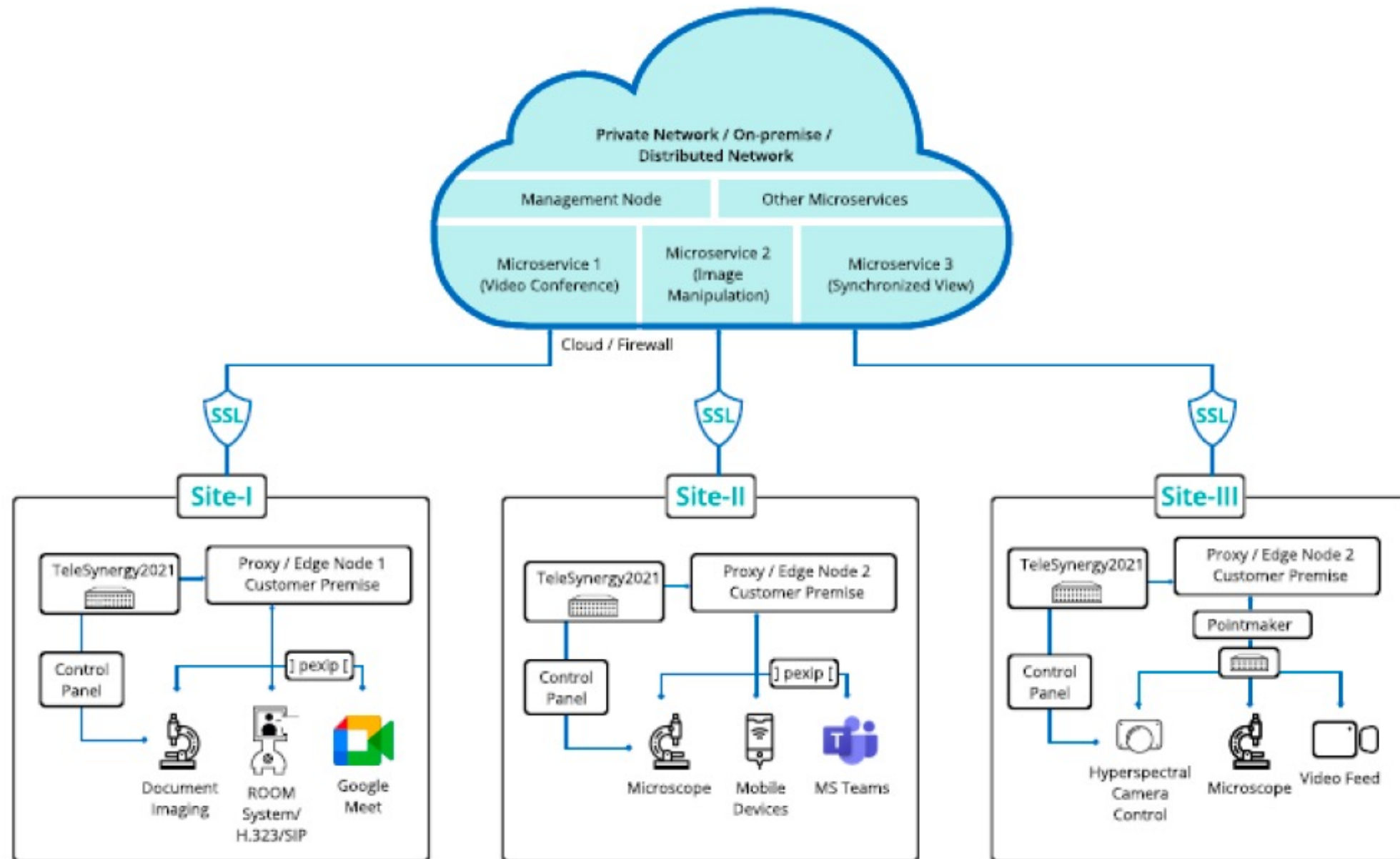


Ireland Site

Telesynergy compared to Video Conference Tools

	Skype/Zoom/GMeet	Telesynergy
Used by NCI for 10+ years	×	✓
High resolution & fidelity in pathology/radiology images	×	✓
Interoperability with different research tools	×	✓
Fully HIPAA compliant	✓	✓
Minimum maintenance	✓	✓

Next generation Telesynergy platform



Considerations regarding potential next steps

