Tumor Panel I:
Rare and Pediatric Cancers

March 17-18, 2015
New York, NY

Tumor Panel I: Rare and Pediatric Cancers

Moderator:

Mike Rice, MS, MBA, Senior Consultant, Defined Health

Panelists:

- *Peter C. Adamson, MD*, Chair, Children's Oncology Group, Alan R. Cohen Endowed Chair in Pediatrics, The Children's Hospital of Philadelphia
- *Meredith K. Chuk, MD*, Scientific Liaison for Sarcoma, Medical Officer, FDA
- *Carlos Rodriguez-Galindo, MD*, Associate Professor, Department of Pediatrics, Harvard Medical School; Medical Director, Pediatric Oncology Clinical Trials, Pediatric Oncology, Dana-Farber Cancer Institute; Director, Solid Tumor Program, Pediatric Oncology, Dana-Farber Cancer Institute
- *Maoxia Zheng, PhD*, Global Development Team Leader, Pediatric Oncology, Genentech
- *Peter Sandor, MD, MBA*, Vice President, Global Marketing Oncology, Amgen Inc.

Pediatric Cancers Largely Treated by Evidence Based / Off-Label Use of FDA Approved Drugs Tested in Adults

- As of 2003, there were only 15 oncology drugs specifically labeled for use in children (Table 1)
- The NCI lists 410 FDA approved oncology therapeutic and supportive care drugs.
- Today, only approximately 20 are FDA approved for pediatric use
  - Only 3 were first approved in children
- According to Adis R&D Insight, there are 67 drugs in development for pediatric oncology indications; which if successful could significantly impact the management of childhood cancers.

Table 1. Fifteen Oncology Drugs Approved for Pediatric Use With Pediatric Dosing Information in the Label

Drug	Indication
L-Asparaginase	Leukemias
Cyclophosphamide	Leukemias, lymphomas, neuroblastoma, retinoblastoma
Cytarabine	Acute nonlymphocytic leukemia in adults and children
Dactinomycin	Wilm's tumor, rhabdomyosarcoma, choriocarcinoma, testicular carcinoma, Ewing's sarcoma, sarcoma botyroides
Daunorubicin	Acute lymphocytic leukemia in adults and children
Doxorubicin	Wilm's tumor, neuroblastoma, soft tissue sarcomas, Hodgkin's disease, other malignant lymphomas, acute lymphocytic leukemia, acute myelogenous leukemia
Lomustine	Brain tumors, Hodgkin's lymphoma
Mercaptopurine	Acute lymphocytic leukemia in adults and children
Methotrexate	Acute lymphocytic leukemia, meningeal leukemia, osteosarcoma, non-Hodgkin's lymphomas
Procarbazine	Hodgkin's lymphoma
Thioguanine	Acute Non-lymphocytic leukemia
Teniposide	Refractory childhood acute lymphocytic leukemia
Tretinoin	Acute promyelocytic leukemia
Vinblastine	Histiocytoses, testicular germ cell carcinomas, Hodgkin's lymphoma
Vincristine	Acute leukemias, lymphomas, Wilm's tumor, rhabdomyosarcoma, neuroblastoma

Journal of Clinical Oncology, Vol 21, No 6 (March 15), 2003: pp 1066-1073, Adis R&D Insight

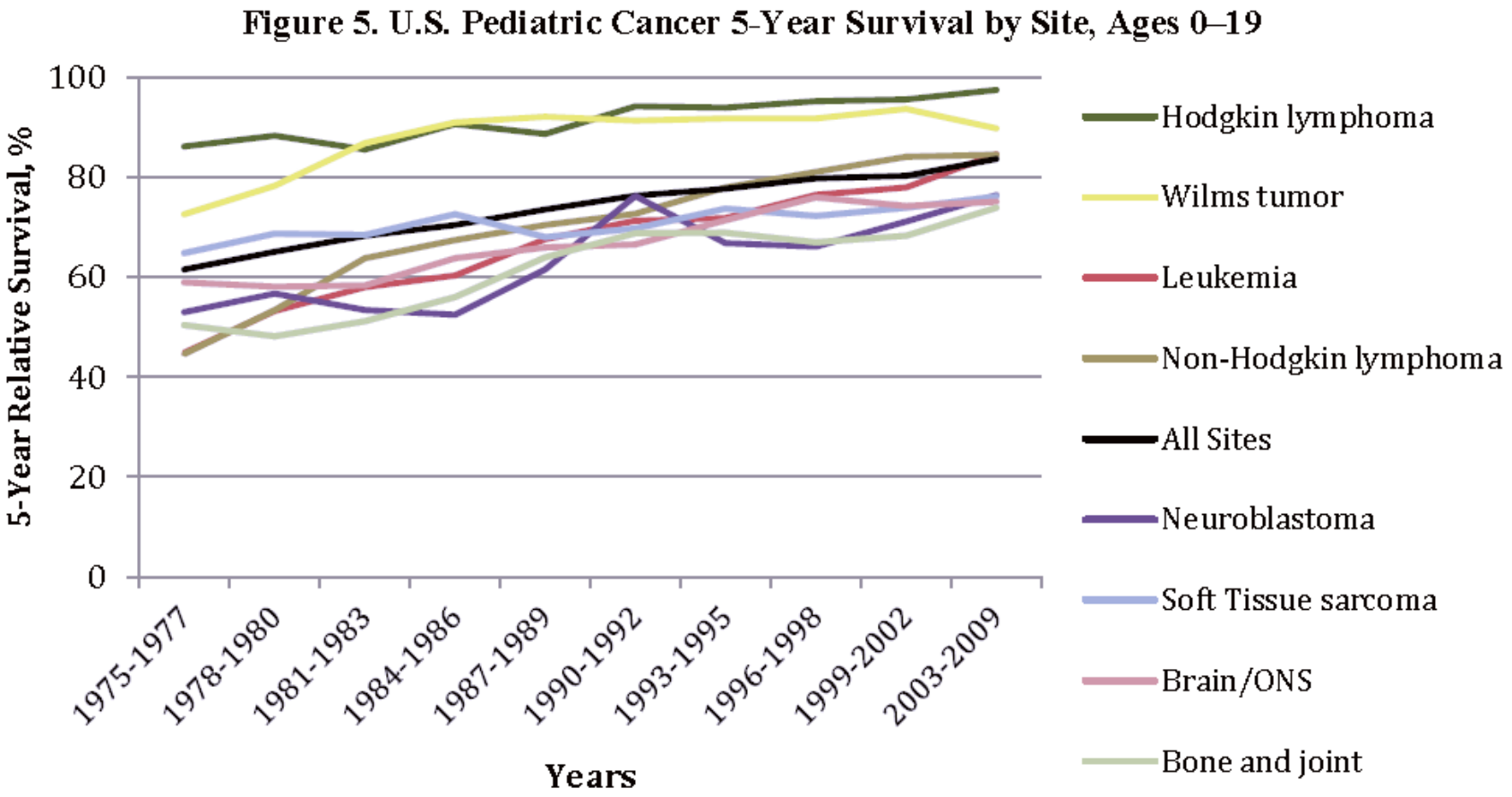
Only 3 Drugs First FDA Approved in Children – Significant Lag for Access to Most Oncology Drugs Approved in Adults

Drug	Pediatric Indication	Pediatric Approval Date	Adult Indication	Adult Approval Date
Unituxin (dinutuximab)	Neuroblastoma	Mar-15	N/A	N/A
Clolar (clofarabine)	R/R ALL	Jan-05	N/A	N/A
Vumon (teniposide)	R/R ALL	Jul-92	N/A	N/A
Arranon (nelarabine)	R/R T-ALL	Oct-05	R/R T-ALL	Oct-05
Oncaspar (pegaspargase)	Front-Line ALL	Jul-06	R/R ALL	Feb-94
Gleevec (imatinib)	Ph1+ ALL	Sep-06	CML	May-01
Affinitor (everolimus)	Tuberous sclerosis complex /subependymal giant cell astrocytoma [Disperz Pediatric Formulation]	Aug-12	R/R RCC TSC /SEGA [Adults and children] Advanced Breast	Mar-09 Mar-10 April 2012

FDA.gov

Despite Limited Innovation in Treating Pediatric Cancers – Incremental Improvements in Protocols Has Reduced Pediatric Mortality By 50%

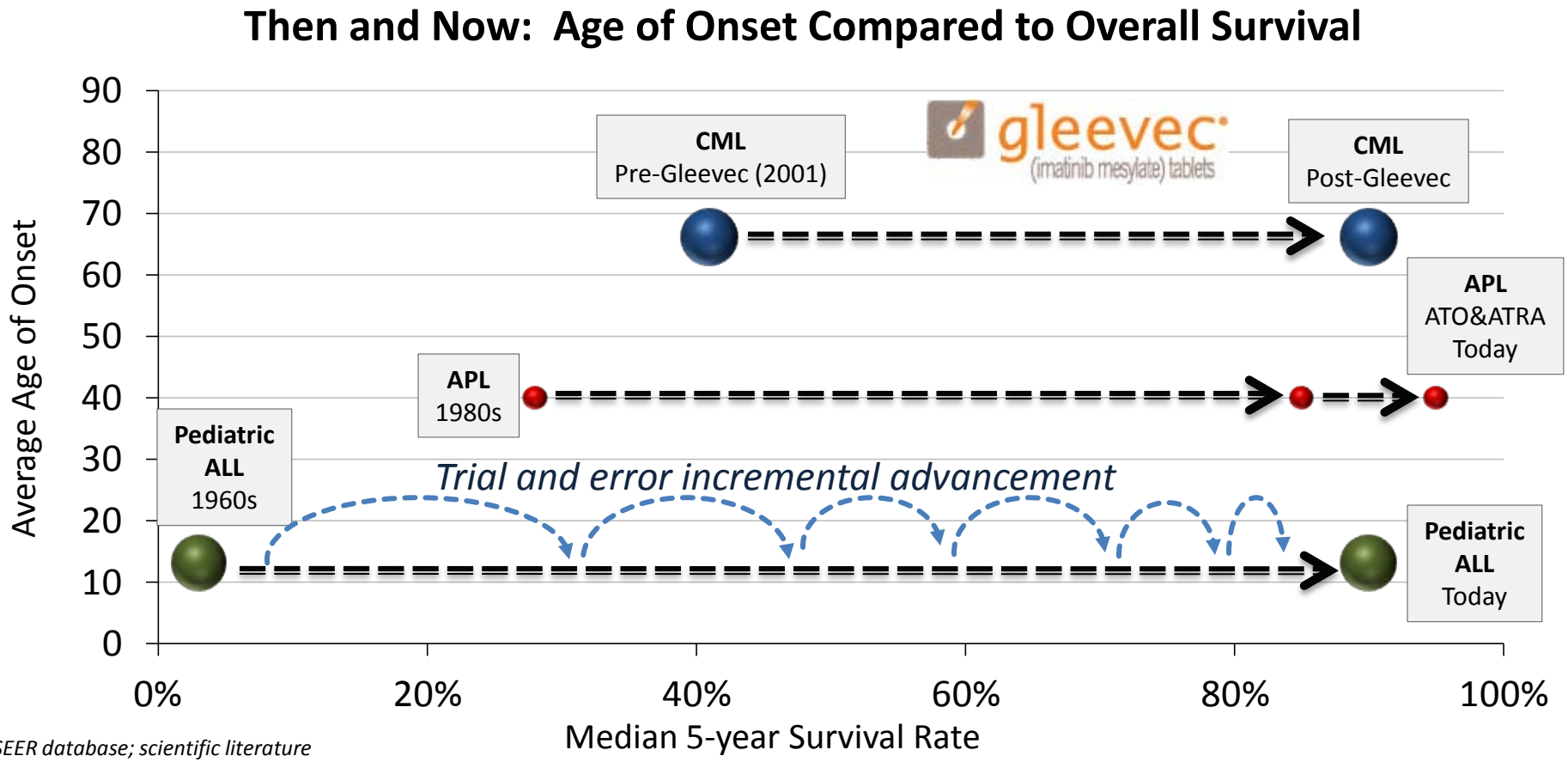
- Cancer is a leading causes of death in children, second only to accidents. (annual 10,450 new cases)



NCI - An Analysis of the National Cancer Institute's Investment in Pediatric Cancer Research, 2013

Outcomes Transformed Through Both Trial and Error and Rationally Designed Transformative Therapies

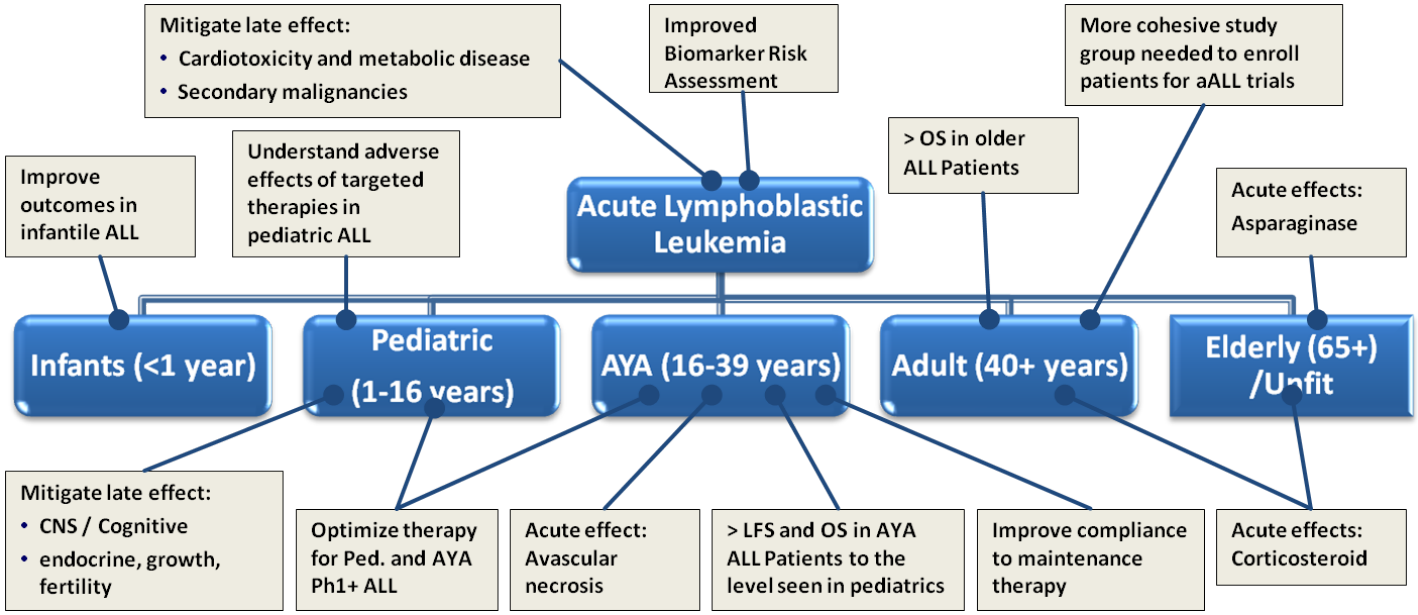
Improvement in patient outcomes can be rapid with rationally designed transformative therapies, or incremental advances in treatment standards



SEER database; scientific literature

Why is it Important to Understand Pediatric Cancer and Prioritize Child Centric Drug Programs?

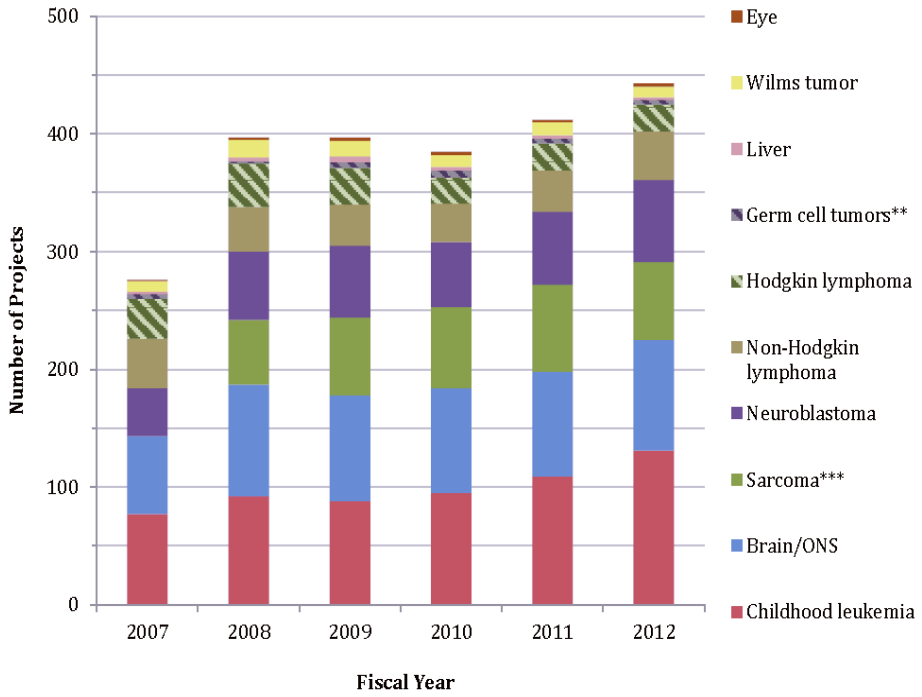
- Cancers in children are distinct diseases compared to those observed in adults
- Compared to adults, children respond differently to therapies and have unforeseen adverse effects:
  - Differences in mutational drivers, relatively few secondary mutations compared to adults
  - Childhood growth and development lead to different toxicities than seen in adult clinical studies (short stature, infertility, cardiotoxicity, cognitive impairment, bone conditions and secondary malignancies)
  - Late effects are different than adults and with median diagnosis at age 6, survivors have >70 years of expected life to deal with sequelae of disease / treatment
- For example, unmet needs in Acute Lymphoblastic Leukemia (ALL) are considerably different depending on age



Aging Formulary of Pediatric Oncology Drugs - How to Incentivize Pediatric Drug Development?

- Most drugs available to children were developed for adult diseases and half the drugs used for pediatric cancer treatment are over 25 years old.
  - The FDA has approved only three new drug expressly developed for a pediatric cancer in the past 25 years.
  - NCI spends 96% of its budget on adult cancers and only 4% of its budget on children's cancers.
- Pharmaceutical companies currently lack the financial incentives to develop new drugs because the market for drugs for rare pediatric diseases is so small.
  - Research and development for new drugs from pharmaceutical companies comprises 60% of funding for adult cancer drugs – almost negligible for childhood cancers.
- NCI's investment in pediatric cancers research was $185.1 million in fiscal year (FY) 2013.

Figure 10. NCI's Childhood Cancer Projects* by Cancer Site



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