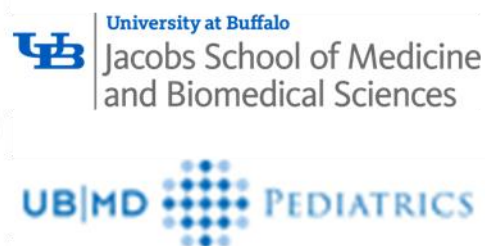


# Pediatric and Adolescent Oncology in Western New York

Childhood Cancer Awareness Month Lecture



**Ajay Gupta, MD, MS**  
Assistant Professor  
Pediatric Hematology/Oncology

September 22, 2021

- At the conclusion of this presentation participants should be able to:
  1. Know the options available to a child, adolescent, or young adult (AYA) with sarcoma in Western New York (WNY)
  2. Know the opportunities to develop new clinical trials and programs for these patients at Roswell Park, Oishei Children's Hospital, and University at Buffalo

# Roswell Park Oishei Children's Cancer & Blood Disorders Program



- Only program of its kind in WNY, combining strengths of two premier specialty centers upstate & WNY's only NCI designated Comprehensive Cancer Center and stand-alone children's hospital
- Allows for increased collaboration on best practices and quality assurance across continuum of pediatric cancer care inpatient and outpatient
- Comprehensive, multidisciplinary team of specialty trained clinicians and support staff, from physicians to nurses, patient navigators and case managers, specializing in all areas of pediatric oncology and hematology





ROSWELL  
PARK®



OISHEI  
Children's



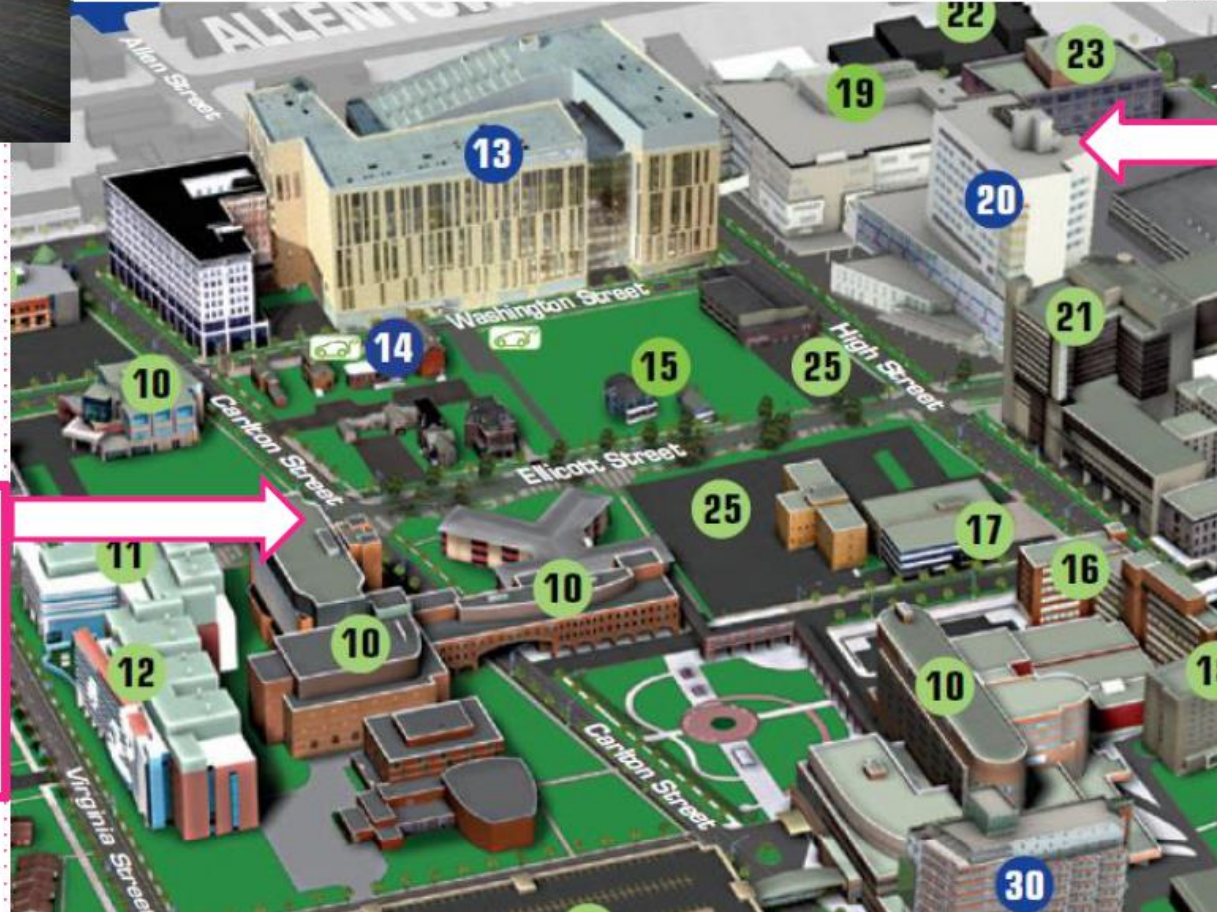
CANCER AND BLOOD DISORDERS PROGRAM

The Ralph C. Wilson, Jr.  
Hematology/Oncology  
Patient Suite at Oishei  
Children's Hospital

The Katherine, Anne  
& Donna Gioia  
Pediatric Center at  
Roswell Park

Chemo-  
therapy  
Infusion and  
Outpatient  
Center

Opened  
September  
2017



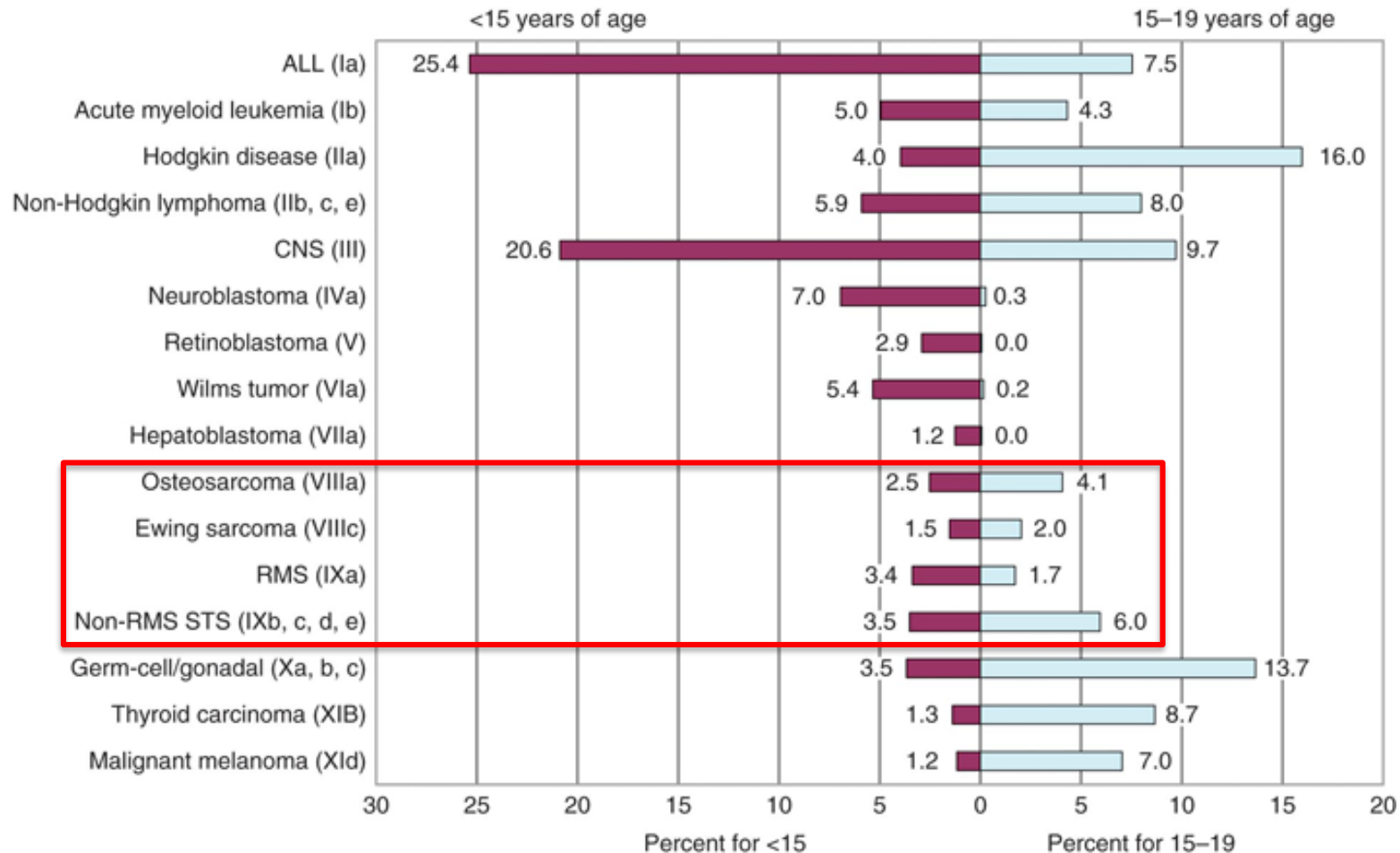
Inpatient  
(including  
BMT)

Opened  
November  
2017





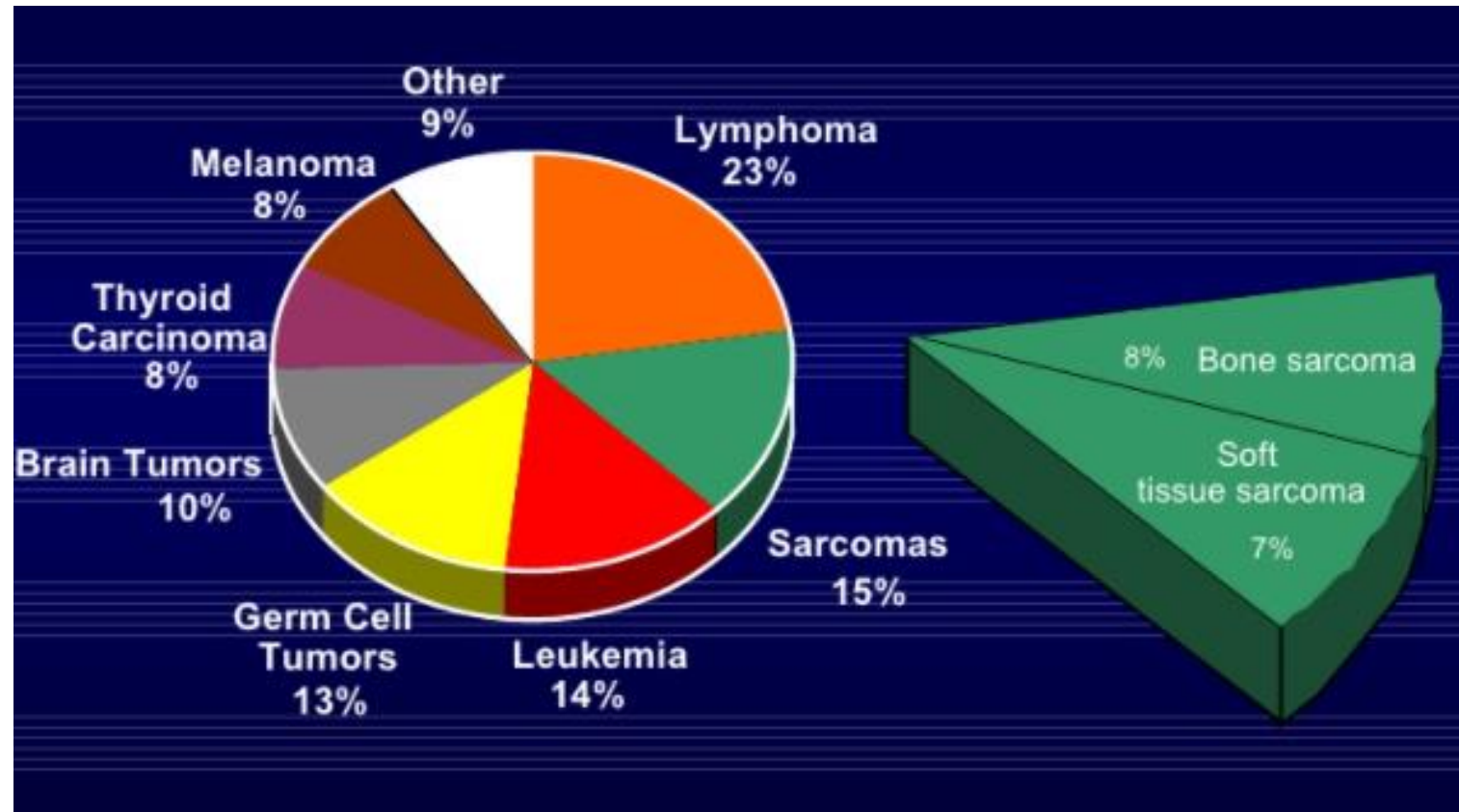
# Pediatric Cancer By Percentage



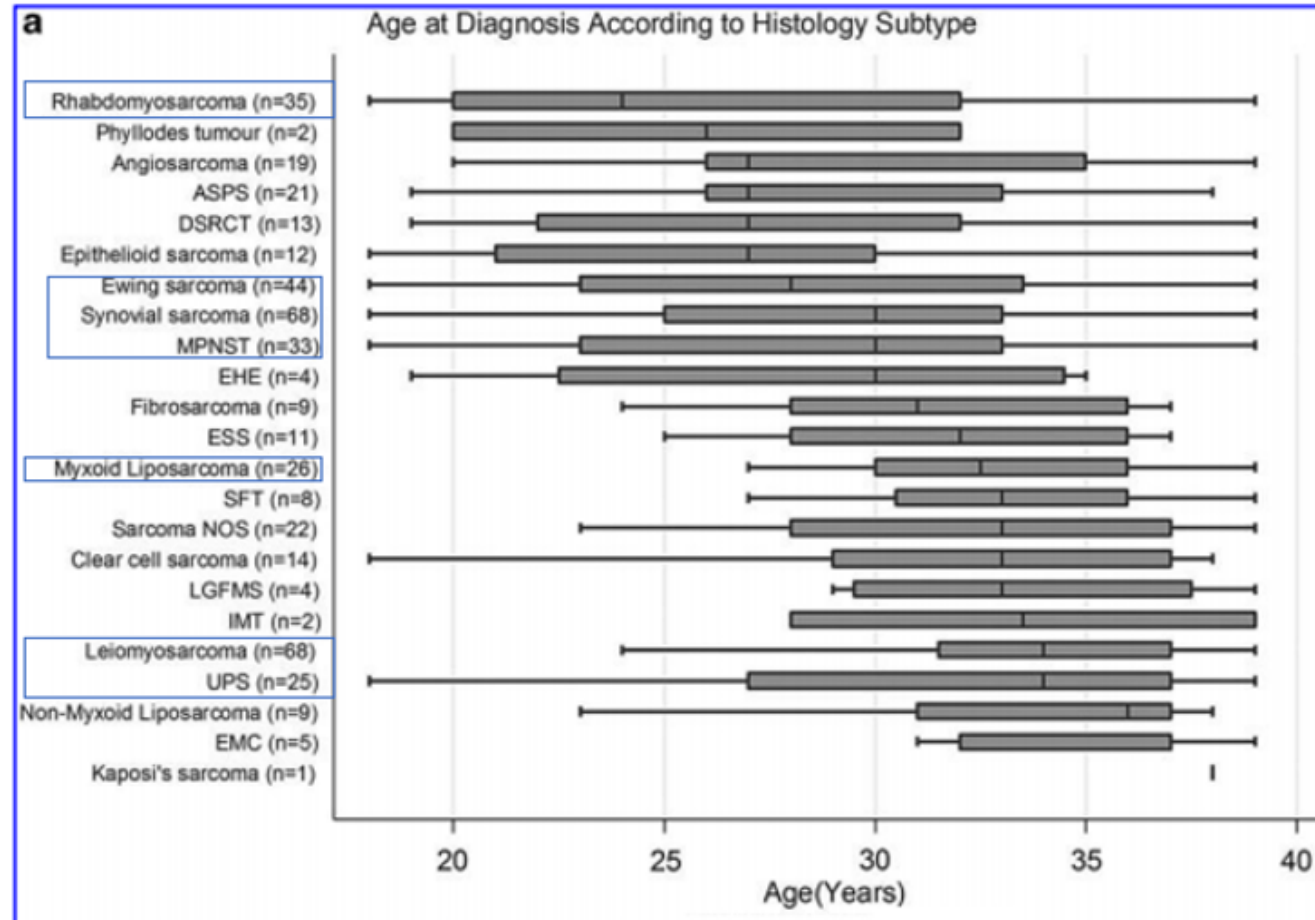
# What is AYA and Why Does it Matter?

- Adolescents and Young Adults (ages 15-39)
- Considered an underserved population with limited focus and resources
- Survival has been shown to improve when these patients are managed by pediatric oncologists
- Many factors at play: diagnosis often delayed, patients less adherent, trials limited, insurance issues, liquid tumors with altered biology, physician lack of expertise

# Adolescent and Young Adult (AYA) Cancer By Percentage



# Soft Tissue Sarcoma in AYA

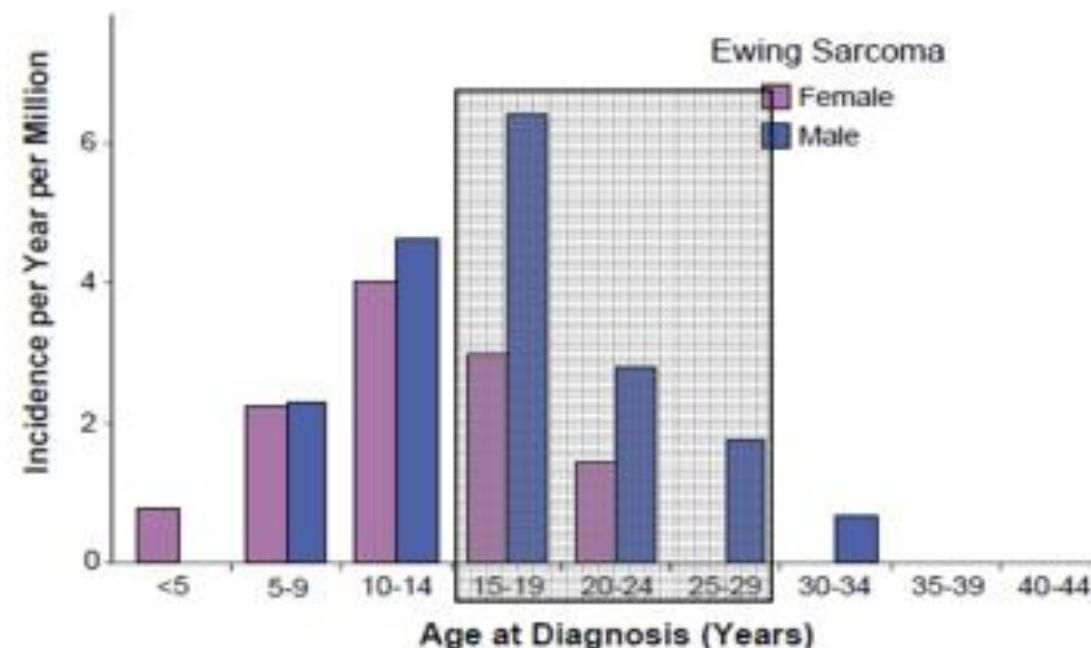




# Sarcomas are Inherently AYA

**TABLE 3.** Estimate of New Cases of Sarcoma in AYA Population in 2004 by Histology

	MDACC AYA	2004 Estimate	
		Total	AYA
Osteosarcoma	38%	1,100	420
Ewing sarcoma (bone/soft tissue)	47%/46%	390/170	180/80
Rhabdomyosarcoma	31%	520	160
Synovial sarcoma	34%	520	175
Neurofibrosarcoma	32%	170	55
Epithelioid sarcoma	33%	170	60
Alveolar soft-parts sarcoma	49%	90	40



# Sarcoma and AYA

- Sarcoma is an ideal model for AYA care, yet outcomes have not improved
- Peak incidences in this age group
- Surgical and Radiation Oncology specialists typically span the AYA population
- Sarcomas are typically treated at large tertiary care centers and CCCs due to rarity (15% of all pediatric cancers, 1% of all adult cancers)
- There is no threshold after which the biology of sarcomas changes abruptly
- Clinical trials are standard of care for the vast majority since standard of care has suboptimal outcomes
- Sarcoma Alliance for Research Through Collaboration (SARC) participates in Children's Oncology Group meetings; CTOS is attended by all

# Current Treatment Strategies

- Neoadjuvant chemotherapy, local control, adjuvant chemotherapy +/- maintenance
- Localized disease has outcomes closer to 65-90%, metastatic disease ~ 10-30%, worse for relapsed/refractory disease

# Clinical Trial Enrollment Needed



## Clinical Research: Drawbacks and common misperceptions

- In USA, only 10% of adolescents are entered to clinical trials sponsored by NCI - not enough patients to make progress.
  - Very little biological data being collected
- In Europe, many adolescents treated in pediatric institutions are entered into co-operative group trials but the entry rate remains low for patients treated outside of established networks.
- Illogical exclusion criteria regarding age eligibility are commonly seen in clinical trials:
  - diseases which cross the pediatric-adult spectrum and yet the trial age-of-entry criteria represent professional boundaries (0-18 or 18-70), not patient needs
- Misperception of poor adolescent compliance to complex protocols.
  - Centres with higher AYA caseloads may enrol a higher proportion of AYA into clinical trials
- False belief that a trial is not needed because of an “excellent” prognosis.

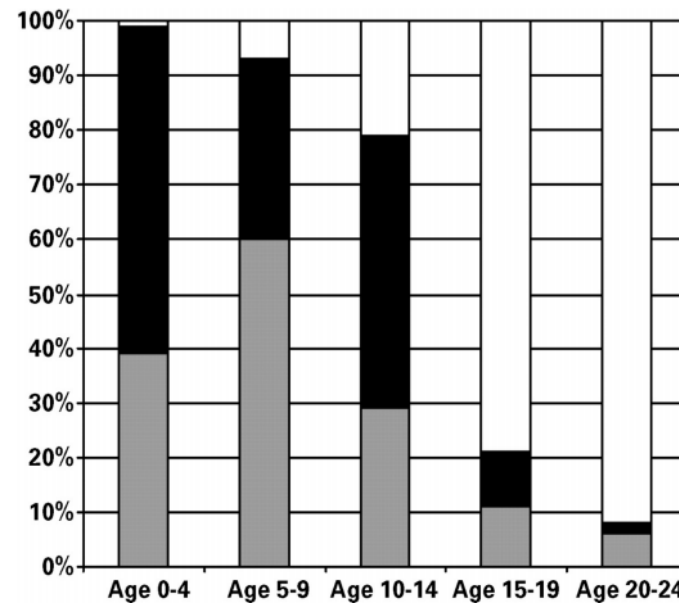
Butow P *et al.* J Clin Oncol 2010;28(32):4800-9  
Whelan JS *et al.* Lancet Oncol 2008;9(4):306-7



# Clinical Trial Enrollment Needed



## Clinical trial participation by age group

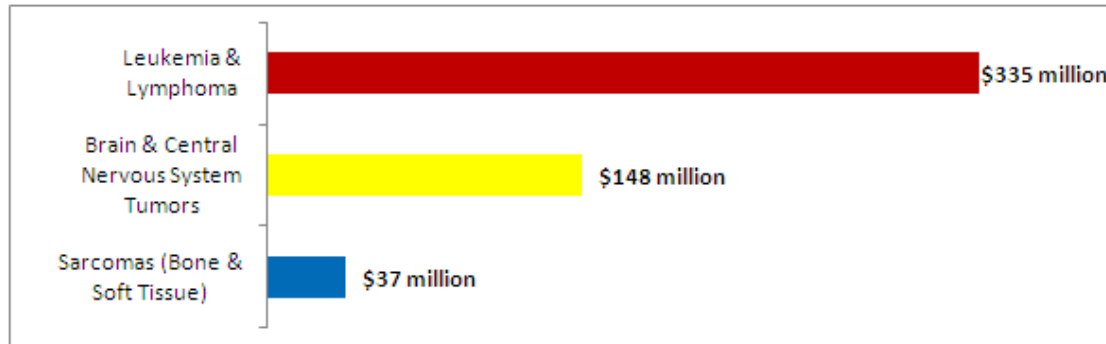


Participation of children, adolescents and young adults with cancer in clinical trials and cooperative treatment protocols in the USA.  
White area: neither protocol nor trial.  
Mid-shading: only cooperative group protocol.  
Darkest shading: entered into both protocol and trial.

SEER data, US National registry 2007  
Pentheroudakis G *et al.* Ann Oncol 2005;16:181-188

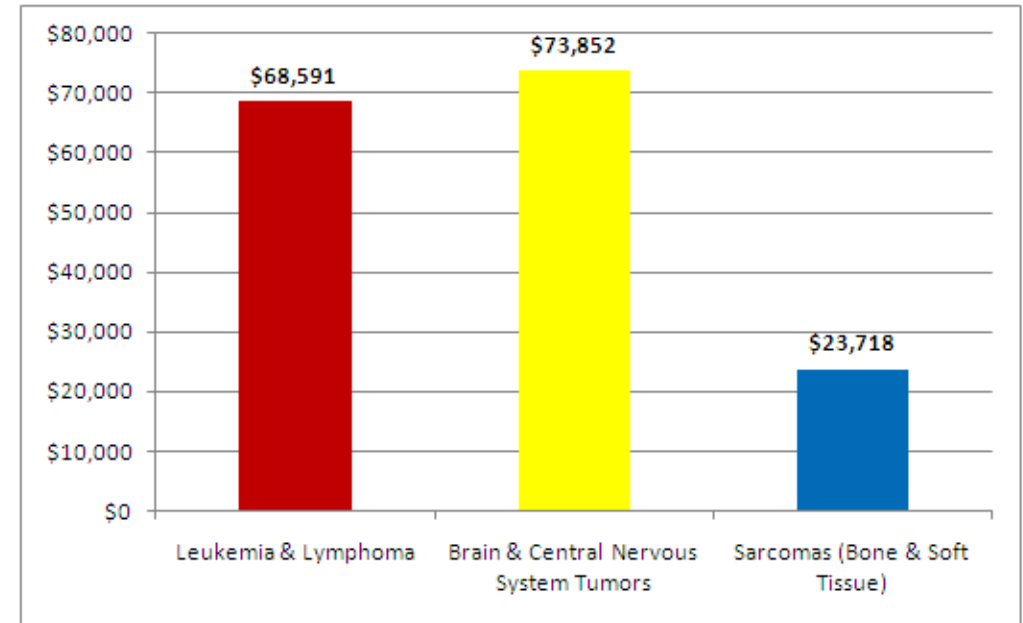
# Sarcoma Funding Needed

Figure 2: NCI Research Funding in 2007



Sources are two NCI publications: 2007 Fact Book (3) and A Snapshot of Sarcoma (4).

Figure 3: National Cancer Institute Research Expenditures in 2007 per newly diagnosed child under 20 years old



This figure uses NCI financials from 2007 (3,4). The number of children diagnosed with each type of cancer is based on SEER percentages from 1975-1995 and totals from 1998 (1).

- Pediatric trained, board-certified Pediatric Hematologist/Oncologist
- Sub-specialty trained in Pediatric Sarcomas
- In Buffalo – Cancer and Blood Disorders Program
  - Department of Pediatric Oncology (Dr. Kara Kelly)
  - Pediatric Developmental Therapeutics (Dr. Clare Twist)
  - Part of the Developmental Therapeutics CCSG (Dr. Igor Puzanov)
- Given broad overlap in age groups for pediatric sarcomas, I see children up to 21 at Oishei and adults up to 35 at Roswell for the same disorders
- Due to Roswell Park Alliance Foundation, I am protected 80% to do clinical research and develop new clinical trials for children with these disorders
- Actively looking for collaborators at Oishei and UBMD

# What is Ajay Doing to Help?

- Biobanking
- Applying for Funding
- Clinical Trial Writing and Opening
- Meeting and Presenting to Interesting Folks
- Joining Consortia
- Marketing Open Trials



# 1. Solid Tumor Biobanking

- Established workflow from Oishei Children's hospital surgical table to Oishei / Roswell tissue biobank
- Established PDX modeling of tumors (Dr. Barbara Foster) based on research interests and also brought in outside models
- Need to establish seed funding

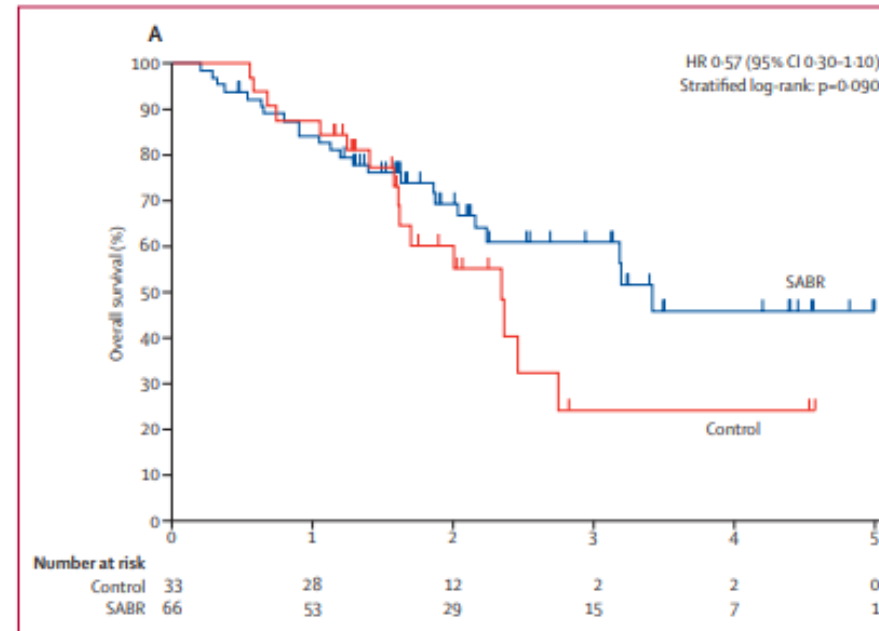
Imaging Dx	Biobanking	PDX
DSRCT	Yes	Yes
Wilms tumor	Yes	Yes
Cystic Brain Tumor	Yes	No
Sacroccocygeal teratoma	Yes	No
Rhabdomyosarcoma, foot	Yes	Yes
Wilms tumor	Yes	No

# 2. SABR for Oligometastatic Disease

- OS 28 months vs 41 months in SABR group
- Median PFS 6 months vs 12 months in SABR group
- Treatment-related deaths in 3 (4.5%) of SABR patients - radiation pneumonitis, pulmonary abscess, subdural hemorrhage after surgery to repair SABR-related perforated gastric ulcer

## Stereotactic ablative radiotherapy versus standard of care palliative treatment in patients with oligometastatic cancers (SABR-COMET): a randomised, phase 2, open-label trial

David A Palma, Robert Olson, Stephen Harrow, Stewart Gaede, Alexander V Louie, Cornelis Haasbeek, Liam Mulroy, Michael Lock, George B Rodrigues, Brian P Yaremko, Devin Schellenberg, Belal Ahmad, Gwendolyn Griffioen, Sashendra Senthil, Anand Swaminath, Neil Kopeck, Mitchell Liu, Karen Moore, Suzanne Currie, Glenn S Bauman, Andrew Warner, Suresh Senan



## 2. SABR for Oligometastatic Disease

- Developed a trial for SABR for pediatric histologies in oligometastatic relapse while at Nationwide Children's Hospital (Columbus, OH)
- Patients  $\geq 3$  years of age excluding radiosensitive tumors
- Currently putting budget together and readying for SRC submission
- Plan is to make Roswell satellite site once up and running at Nationwide

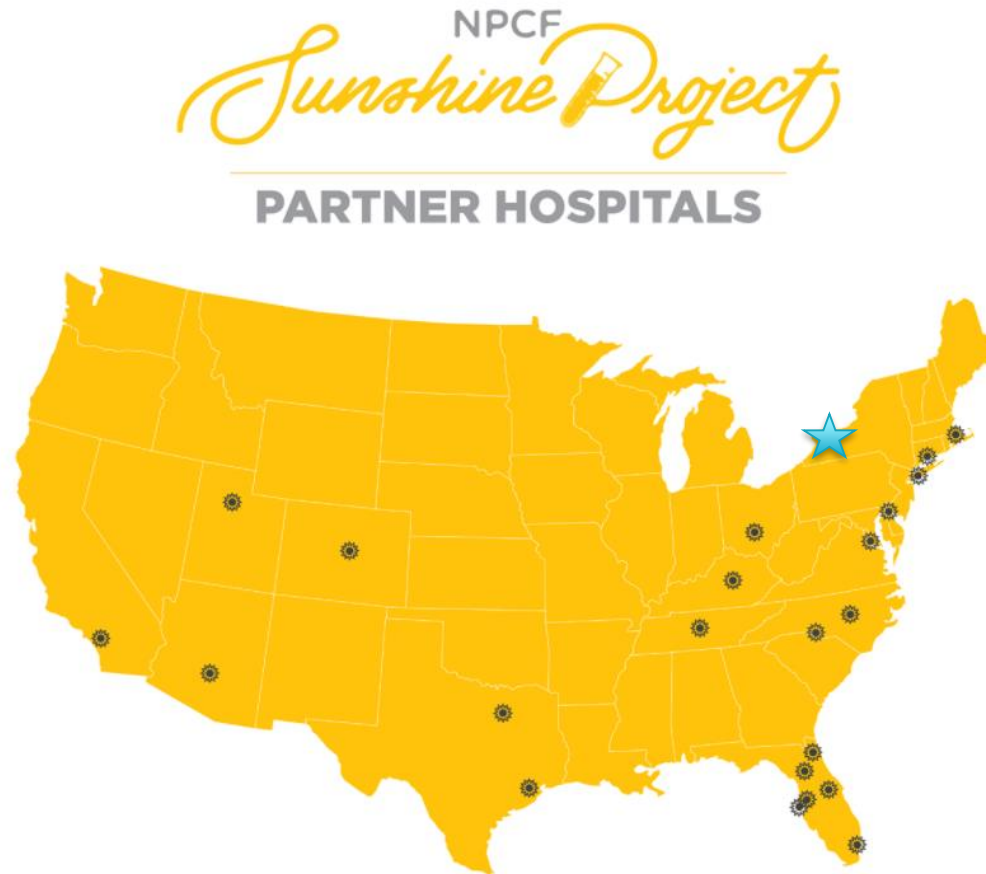
# 3. Replication Stress in Ewing Sarcoma

- Ewing sarcoma (ES) has elevated genomic instability and DNA-RNA binding (R-loops) known as replication stress
- There is an S-phase kinase known as CDC7 (aka DDK) whose increased activity in Ewing sarcoma replication is dependent on EWSR1-FLI1 fusion
- Inhibiting this kinase (DDKi) causes mitotic catastrophe in ES (Ohm)
- Collaboration with MSKCC to explore 2 and 3-compound drug screen with agents active in relapse, PDX modeling
- Received 2-year funding for this through Hyundai Hope on Wheels Young Investigator award this month



# 4. Sunshine Project

- Biomarker trial open that includes fusion-positive sarcoma patients up to 40 years old
- Opening 2 additional trials
  - Nivolumab / Azacitadine for resectable, relapsed osteosarcoma
  - Evolution trial for high-risk rhabdomyosarcoma



Children's Hospital of Los Angeles, Los Angeles, CA  
Connecticut Children's Medical Center, Hartford, CT  
Nemours/Alfred I du Pont Hospital for Children, Wilmington, DE  
UF Health Shands Children's Hospital, Gainesville, FL  
Nemours Children's Clinic, Jacksonville, FL  
University of Miami Sylvester Cancer Center, Miami, FL  
Holtz Children's Hospital, Miami, FL  
Johns Hopkins All Children's Hospital, St. Petersburg, FL  
Primary Children's Medical Center, Salt Lake City, UT  
Moffitt Cancer Center, Tampa, FL  
University of Kentucky Markey Cancer Center, Lexington, KY  
Children's Hospital Colorado, Aurora, CO  
Dana-Farber Cancer Institute, Boston, MA  
Johns Hopkins Medicine, Baltimore, MD  
Carolina's Medical Center/Levine Children's Hospital, Charlotte, NC  
University of North Carolina Cancer Hospital, Chapel Hill, NC  
The Children's Hospital at Montefiore, Bronx, NY  
Nationwide Children's Hospital, Columbus, OH  
Phoenix Children's, Phoenix, AZ  
Vanderbilt-Ingram Cancer Center, Nashville, TN  
Nemours Children's Hospital, Orlando, FL  
University of Texas MD Anderson Cancer Center, Houston, TX  
Children's National, Washington, DC  
Children's Health, Dallas, TX

# 5. Marketing Available Trials



CANCER AND BLOOD DISORDERS PROGRAM

## Early Phase Clinical Trials

Summer 2021

### *Relapsed / Refractory*

#### SOLID TUMORS

**LOXO-RET-17001**  
Phase 1/2 Study of LOXO-292 in Patients With Advanced Solid Tumors, RET Fusion-Positive Solid Tumors, and Medullary Thyroid Cancer  
<https://www.roswellpark.org/clinical-trials/list/4023>  
Phase I      Open to ages ≥12 yr  
PI: Grace Dy  
Contact: Clare Twist  
Clare.Twist@RoswellPark.org

**Only Site Update**

#### LEUKEMIA/LYMPHOMA

**DFCI 18-328**  
Ribociclib in Combination With Everolimus and Dexamethasone in Relapsed ALL  
<https://www.roswellpark.org/clinical-trials/list/4285>  
Phase I      Open to ages 1 yr to 30 yr  
PI: Clare Twist  
Clare.Twist@RoswellPark.org

**COG AALL1621**  
A Phase 2 Study of Inotuzumab Ozogamicin in Children and Young Adults with Relapsed or Refractory CD22+ B-Acute Lymphoblastic Leukemia (B-ALL)  
<https://www.roswellpark.org/clinical-trials/list/3635>  
Phase II      Open to ages 1 yr to 21 yr  
PI: Clare Twist  
Clare.Twist@RoswellPark.org

**Only Site Update**

- **COG AALL1721 - A Phase II Trial of Tisagenlecleucel in first-line high risk (HR) Pediatric and Young Adult Patients with B-Cell Acute Lymphoblastic Leukemia) Who are MRD positive at the End of Consolidation Therapy**
- **BMT CTN 1507 - Reduced Intensity Conditioning for Haploidentical Bone Marrow Transplantation in Patients with Symptomatic Sickle Cell Disease**

# 6. Other Germinating Ideas

- HIPEC for AYA patients
- TILs in pediatric histologies (Moffitt)
- Pulmonary suffusion of drug in CF (Demmy)
- Other interesting compounds
  - Alpha-1 dendritic cells plus checkpoint inhibition (Kalinski) – pediatric cell lines in hand
  - Curaxins / CBL0137 (Gudkov)
  - Cicloprox, teniposide (Gelman)
  - Oncolytic viruses (Tim Cripe, Nationwide)
  - Survaxin (Fenstermaker)
  - Propanolol (Repasky)
  - Pharma/Industry collaborations
- Correlative studies
  - Bob Straubinger / Don Mager (liposomal irinotecan PK/PD)
- MatchTX algorithmic output
- Omniseq
- Database mining for preliminary data (genomic, radiomic, etc)
  - Roswell Oishei Pediatric and AYA Registry
  - INSTRuCT (Volchenbaum, UChicago)
  - dbGaP (Childhood Cancer Survivor Study)
  - TARGET, UCSC Treehouse, St. Jude PECAN, cBioPortal/PedscBioPortal
- Precision medicine consult service
- EPCT concierge service
- Online presence (Twitter/joint venture website/outreach/portal development)

# Increasing Cross-Collaboration

- Can connect you to cell lines / PDX models for pediatric solid tumors
- Can write collaborative grants based on shared interests
- Can bring your novel ideas to wider / different audience





**IDEAS  
WHAT'S NEXT?**