Sylvester Precision Medicine Basket Trials and Phase I Trials

Dr. Reshma L. Mahtani
Associate Professor, Division of Hematology/Oncology

October 30, 2018

SYLVESTER COMPREHENSIVE CANCER CENTER
UNIVERSITY OF MIAMI HEALTH SYSTEM

IN PURSUIT OF *YOUR CURE.*™

NCI- MATCH

Agent	Mutation
Afatinib	EGFR activating mutation
Crizotinib	MET exon 14 deletion
Osimertinib	EGFR T790M or rare activating mutation
Crizotinib	ALK translocation
Crizotinib	ROS1 translocation or inversion
TAK228 (MLN0128)	mTOR
TAK228 (MLN0128)	TSC1 or TSC2
Trametinib	GNAQ or GNA11 mutation
Vismodegib	SMO or PTCH1 mutation
Sunitinib malate	cKIT exon 9, 11, 13, or 14 mutation
Palbocicilib (Ibrance)	CDK4 and CDK6 amplifications
LOXO-101	NTRK1, 2, or 3 fusion
Copanlisib	Deleterious PTEN (NGS) and PTEN pos (by IHC)

- MATCH is a multi-arm basket trial
  - Disease-type agnostic
  - Enrollment is based on mutations
- Combination of FDA approved and experimental drugs
- MATCH is a trial adapting to results
  - After some findings arms have close and others have opened

Original arms still open

MATCH: New and Opening Arms

- **5 Arms opened in July 2018**
  - Data from ASCO ’18 led MATCH to modify their arms, and added 2 new drugs

Agent	Mutation
Erdafitinib	FGFR amp
Erdafitinib	FGFR mutations or fusions
Copanlisib	PIK3CA
Copanlisib	PTEN loss (by IHC) w/ PIK3CA mutation
Copanlisib	Deleterious PTEN (NGS) and PTEN pos (by IHC)

- **Three more arms are slated to open December 2018**

Agent	Mutation
AZ1775	TP53 mutation and MYC amp
Ipatasertib	AKT mutation
Ulixertinib	Non-V600 BRAF

ASCO TAPUR

Agent	Mutations
Dasatinib (Sprycel)	Bcr-abl, SRC, KIT, PDGFRB, EPHA2, FYN, LCK, YES1 mutations
Nivolumab and Ipilimumab (Opdivo and Yervoy)	MSIH, high mutational load MLH1, MSH2, MSH6, PMS2, EPCAM, BRCA1, BRCA2, ATM, MSH3, PMS1, MLH3, EXO1, RFC1-5, PCNA, RPA1-4, SSBP1
Olaparib (Lynparza)	BRCA1/BRCA2 inactivating mutations; ATM mutations or deletions
Pembrolizumab (Keytruda)	POLE/POLD1, high mutational load over 9 mut/Mb
Regorafenib (Stivarga)	RET, VEGFR1, VEGFR2, VEGFR3, KIT, PDGFRβ, RAF-1, BRAF mutations/amplifications
Trastuzumab and Pertuzumab (Herceptin and Perjeta)	ERBB2/ERBB3 amplifications, overexpression, or documented ERBB2 pathogenic mutations
Vemurafenib and Cobimetinib (Zelboraf and Cotellic)	BRAFV600 mutations

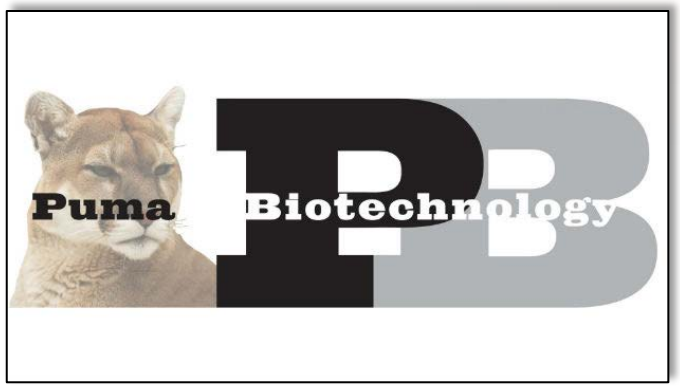
- TAPUR is also a multi-arm basket trial
  - Enrollment is based on mutations
  - Multiple disease types eligible on each arm
  - Multiple mutations eligible per arm
- FDA approved treatments only
  - investigating new indications for drugs already available
- Sponsored by major pharmaceutical companies

TAPUR: Adapting to results

- As results are returned arms are modified or completely closed to reflect discovered efficacy of the agents
- These arms are still open but have limited their cohorts to disease types that may benefit the most, based on findings

Agent	Cohorts open
Cetuximab (Erbitux)	Ovarian Ca. - KRAS, NRAS and BRAF wildtype
Palbociclib (Ibrance)	Peritoneum, retroperitoneum - CDK4 amp Lung – CCND1 amp Head and Neck, ovarian - CDKN2A loss or mutation Soft tissue sarcoma – CDK4 amp, CDKN2A loss or mutation
Sunitinib (Sutent)	Breast cancer – FGFR1, FLT3 mutations or amp Bone and Cartilage, Colorectal – FGFR1 Lung, Gall bladder, Bile duct – FGFR2

Additional Precision Medicine Phase II Basket Trials



- **PUMA Summit Trial**
  - Targeting: ERBB2/4 (HER2/4), EGFR (exon 18)
  - Agent: Neratinib
  - SDGs: Colon cancer, lung cancer, breast cancer and bladder cancer

- **BluePrint RET Trial**
  - Targeting: RET mutated cancers
  - Agent: BLU-667 (RETi)
  - SDGs: Solid Tumors

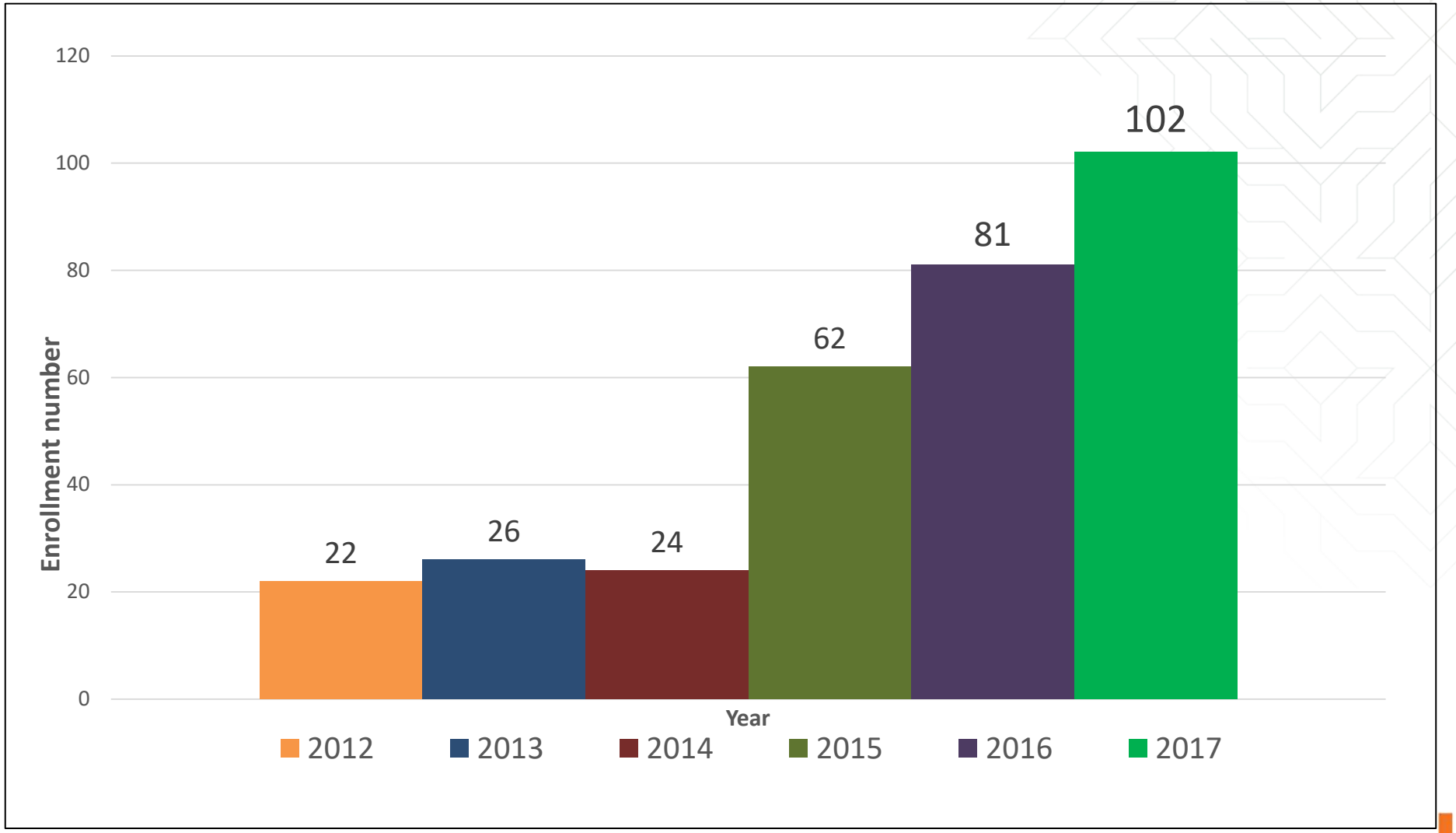
Phase I Clinical Trials

Phase I Clinical Trials

- Sylvester's robust clinical trial portfolio offers options to late stage cancer patients
- Enrollment in phase I is strong and Sylvester is also very efficient at activation of new trails
- Phase I collaborates with Precision Medicine to identify clinical trials that may provide benefit to our patient population

Agent	Indications
PLX9486 (c-KIT inhibitor) + Sunitinib (Part 2e)	Solid tumors (including GIST)
Toca 511 (retroviral replicating vector) + Toca FC (flucytosine)	Advanced solid tumors or lymphoma
AGEN1884 (CTLA-4 inhibitor)	Advanced / Refractory tumors
VSV-IFNβ-NIS (modified vesicular stomatitis virus)	Refractory solid tumors
Corvus: CPI-006 (single agent) or in combo w/ CPI-444 or Pembro	Advanced solid tumors
Celldex: CDX014 anti-CD40 monocolonal antibody	Advanced Solid Tumors
FORMA: FT-2102 monotherapy or combination (advanced solid tumors + gliomas w/ IDH1 mutation)	All R/R Solid Tumors

Phase I Enrollment 2012 -2017



SYLVESTER COMPREHENSIVE CANCER CENTER
UNIVERSITY OF MIAMI HEALTH SYSTEM
IN PURSUIT OF *YOUR CURE.*™

Thank You

SYLVESTER
COMPREHENSIVE CANCER CENTER
UNIVERSITY OF MIAMI HEALTH SYSTEM

IN PURSUIT OF *YOUR CURE.*™