NCI National Clinical Trials Network (NCTN)

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NIH NATIONAL CANCER INSTITUTE

National Cancer Advisory Board

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Transformation of former Cooperative Group program into NCI National Clinical Trials Network (NCTN) 2014

Establish/Support programmatic infrastructure to:

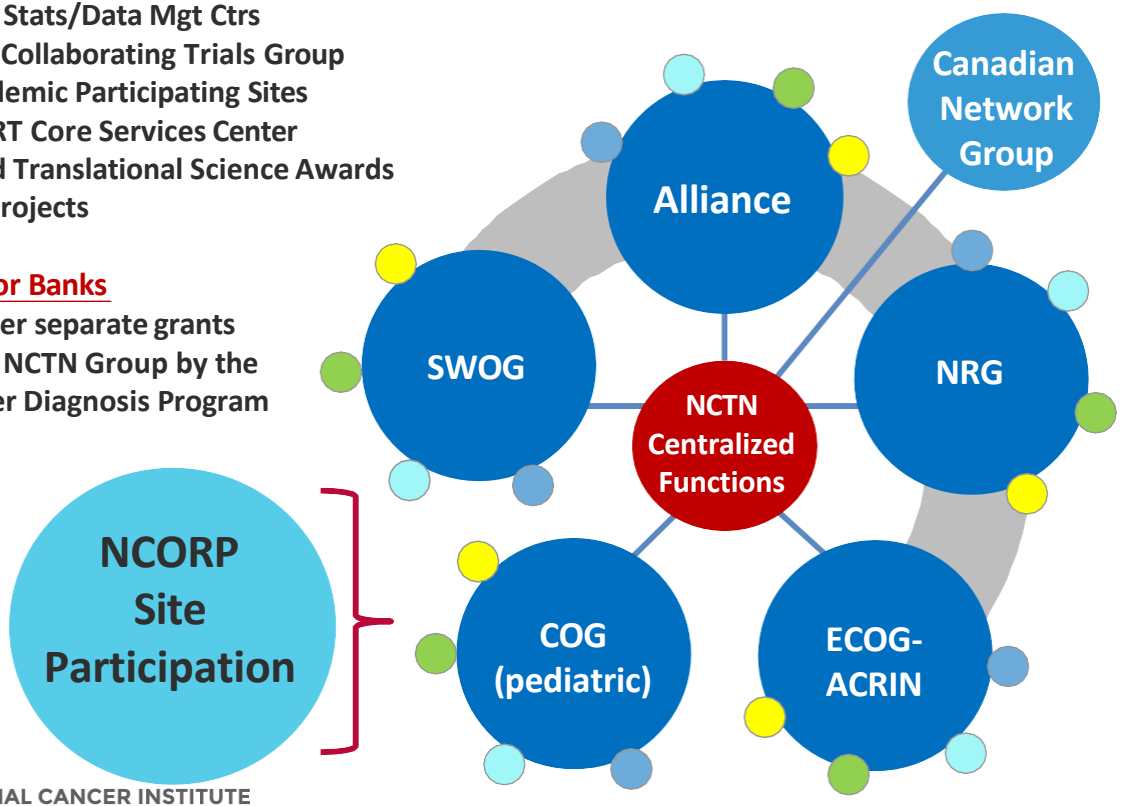
- ✓ Harmonize processes & promote collaborations
- ✓ Focus on questions not well supported in commercial environment
- ✓ Prioritize trials & incorporate innovative science and design
- ✓ Provide large-scale testing of molecularly-defined cancers & incorporate "*precision medicine"* into portfolio, along with rare tumor trials
- ✓ Maintain commitment to conduct trials in diverse & special populations

NCTN Program Organizational Structure

6 Main Components:

- US Group Operation Ctrs
- US Group Stats/Data Mgt Ctrs
- Canadian Collaborating Trials Group
- Lead Academic Participating Sites
- Imaging/RT Core Services Center
- Integrated Translational Science Awards for pilot projects

NCTN Tumor Banks
funded under separate grants for each US NCTN Group by the DCTD Cancer Diagnosis Program



LEGEND:

Centralized Functions:
- NCI CIRB with 4 Boards
- Cancer Trials Support Unit
  - Investigator Credentialing
  - 24/7 Enrollment Coverage
  - Regulatory Monitoring
- RT/Image Core Ctr (IROC)
- NCI Steering Committees
- Common Data Mgt System w/ Central Hosting (RAVE)

Lead Academic Participating Sites (LAPS)

Operations Centers

Statistics & Data Mgt

Tumor Banks

CORE Infrastructure for Clinical Trials Supports NCTN
& Other NCI-funded clinical trials networks

Contract support in following domains:

- ✓ **Information Security**
- ✓ **Study Administration & Logistics**
- ✓ **Clinical Data Capture & Reporting**
  - ❖ Enrollment, Medidata Rave Mgt System
- ✓ **Regulatory Monitoring & Reporting**
  - ❖ Investigator Credentialing
  - ❖ NCI CIRB & Regulatory Support
  - ❖ IND Sponsor Activities on Select NCTN Trials
- ✓ **Data Quality & Control**
- ✓ **Correlative Study Data**

NCTN Program Organizational Structure

Large Umbrella/Basket Trials Requiring National Catchment Area

ComboMATCH (Combination Targeted Therapies in Various Cancers)

myeloMATCH (Series of for patients from dx thru *all* stages of AML/MDS)

iMATCH (Pilot platform for molecular testing to enhance I/O therapy trials)

All with Central Molecular Characterization Laboratories

Multimodality & Non-Drug Trials

Role of Weight Loss in Treatment of Early Breast Ca

Dose-Escalated RT +/- ADT in Intermediate Prostate Ca

Combination Therapy Trials

Chemo + Immunotx in Resected Stage III Colon Ca dMMR

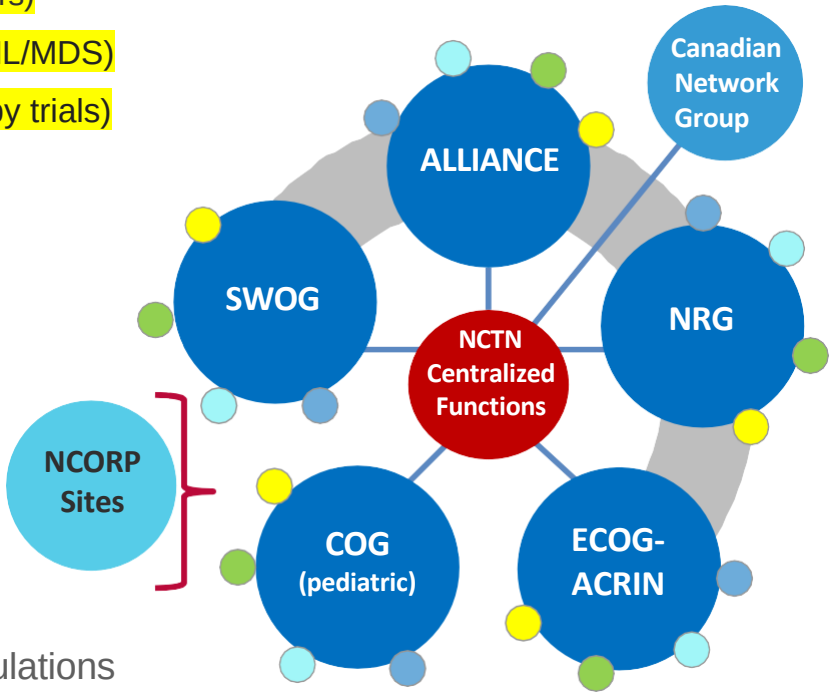
Special Populations & Initiatives

AYA Trials, Broadening Eligibility & Outreach to Diverse Populations

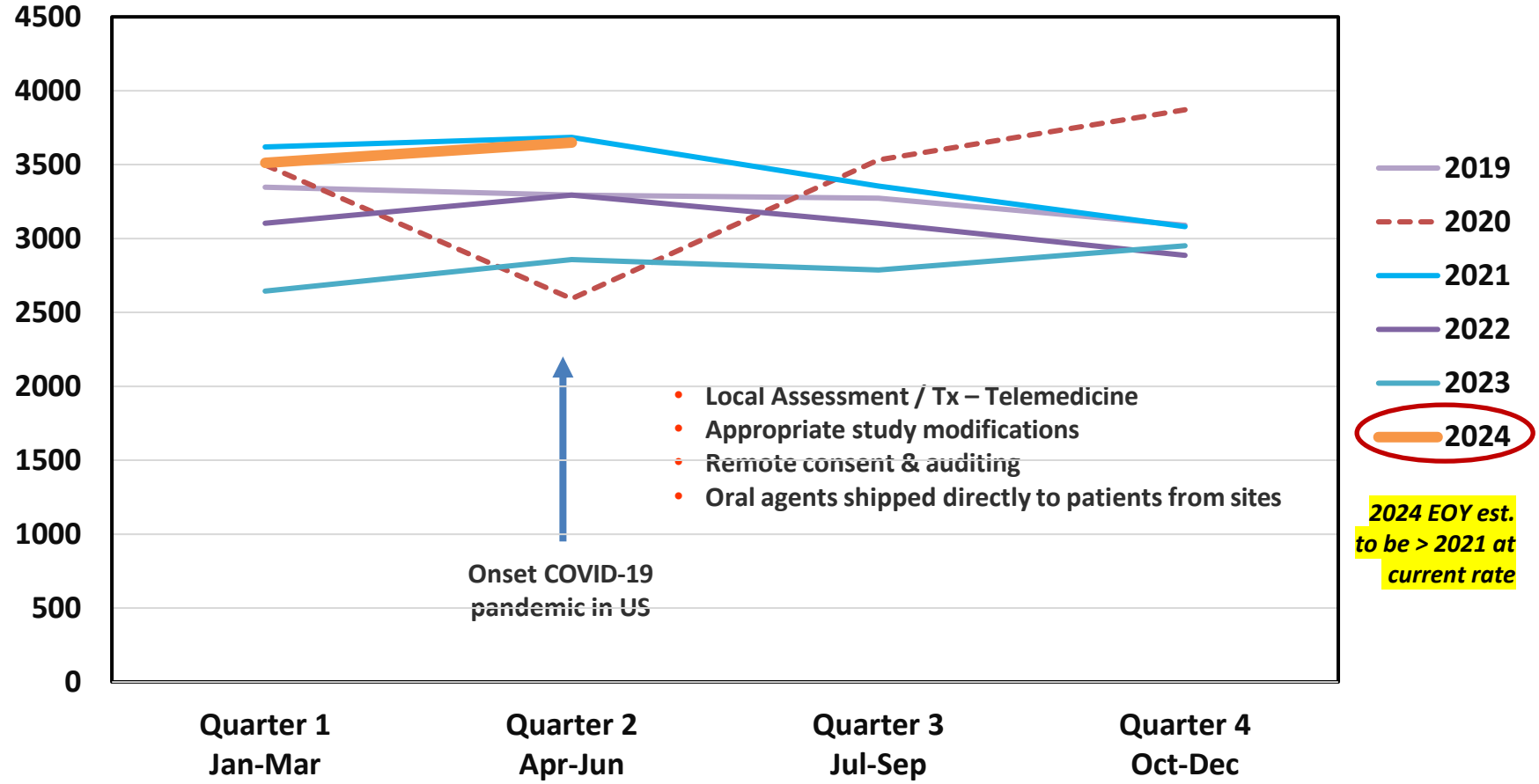
Streamlining Clinical Trials & Decentralized Clinical Trials

NCTN/NCORP Data Sharing Archives & Biospecimen Access

Real World Trials: Pragmatica-Lung



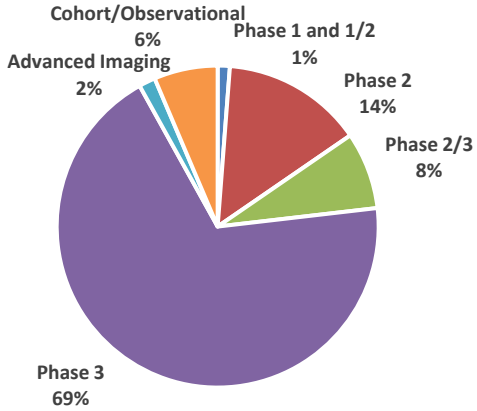
NCTN Quarterly Intervention Accrual January 2019-June 2024



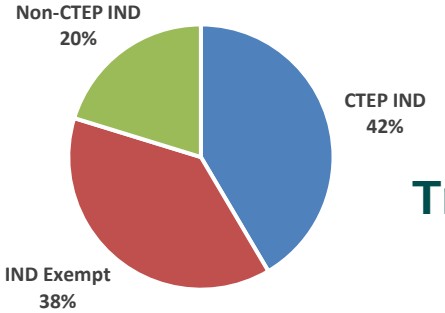
Intervention/Cohort Accruals: Trial Phase, IND, & Cancer Type

(3/1/2019 to 7/31/2024)

Trial Phase

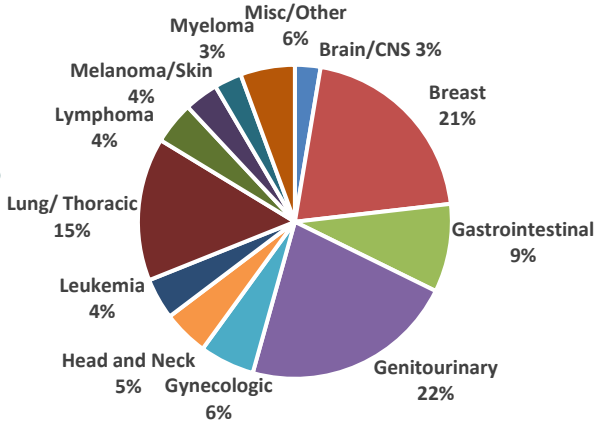


Trial IND Type



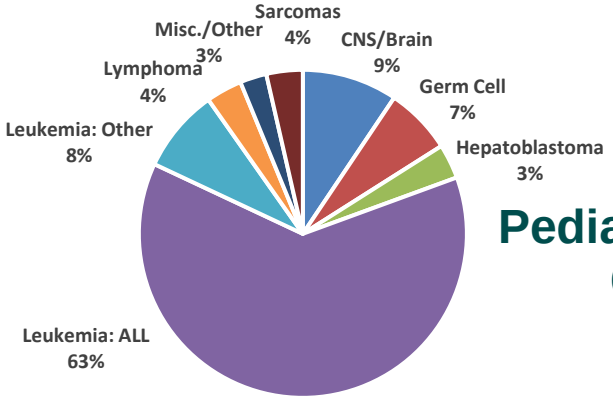
Adult Cancers

(n=59,273)



Pediatric Cancers

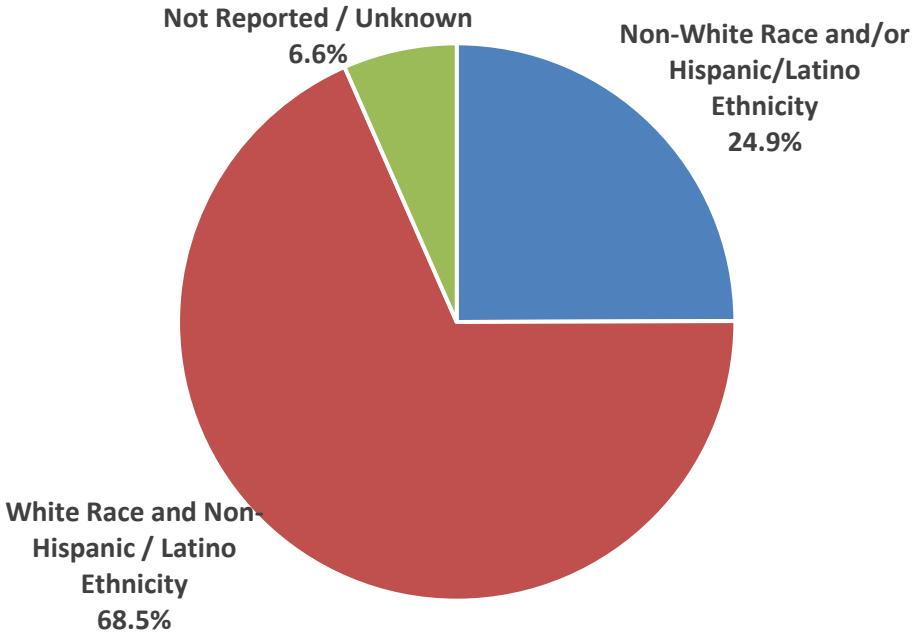
(n=13,504)



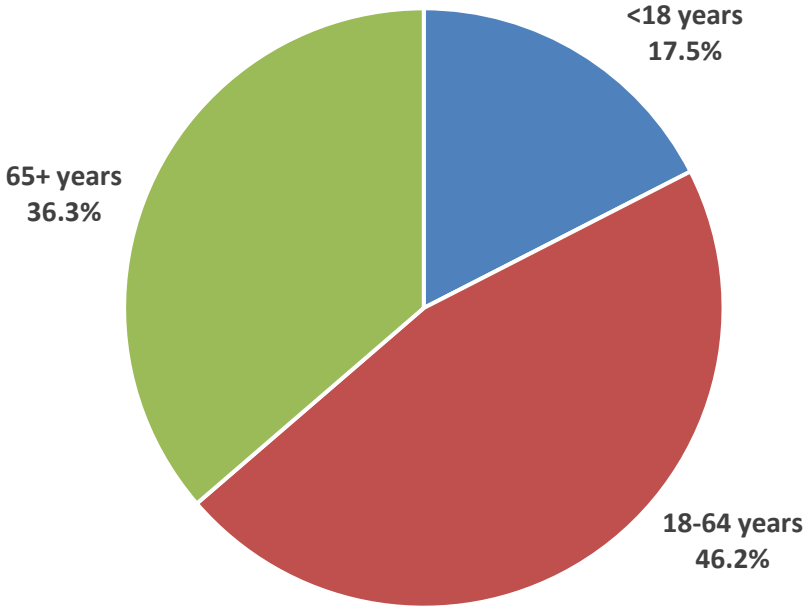
Intervention/Cohort Accruals: Demographic Overview

(3/1/2019 to 7/31/2024)

Patient Race and Ethnicity



Patient Age



Approx 16% of patient enrolled come from Rural Areas as of 10/22/22: This is between US Census est. of 19.3% of US populations & OMB estimate of 15%

NCTN Study Components & Accrual

	Study Component & Accrual by Project Period	
NCTN Study Component	3/2014-2/2019 (60 Months) "Annual Avg"	3/2019-7/2024 (65 Months) "Annual Avg"
# LOI & Concept Approval	51	44
# Trial Activations	46	39
NCTN Accrual Component	3/2014-2/2019 "Annual Avg"	3/2019-7/2024 "Annual Avg"
# Accruals: Screen on Study	5,494	3,960
# Accruals: Intervention/Cohort	15,180	13,551
# Accruals – Total Accrual	20,674	17,511

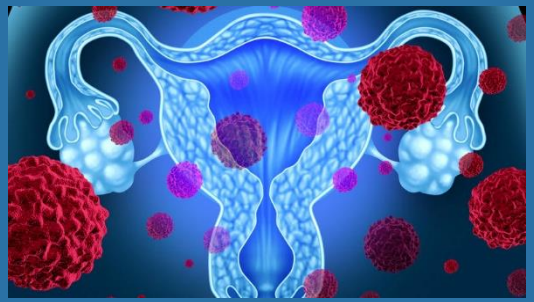
Period 1 "Screening on Study" accruals include the large Adult & Pediatric MATCH Precision Medicine Platform Trials
Period 2 "Intervention Accrual" decreased by ≈10.7% due to COVID-19 pandemic

Key Accomplishment:
Incorporate Innovative Science & Design into Clinical Trials

FDA Approval on June 17, 2024: Pembrolizumab in Endometrial Ca

NRG-GY018: Phase 3 Randomized Placebo-Controlled Study of Pembrolizumab Added to Paclitaxel & Carboplatin for Measurable Stage III or IVA, Stage IVB, or Recurrent Endometrial Cancer

N Engl J Med. 2023; 388(23):2159-2170



Study Opened: Jul 2019
Study Closed: Dec 2022
819 Patients Enrolled

M/F: 0% / 100%
White 79%, Black 15%, Asian 5%,
Other 1% - Hispanic 6%

Measurable Stage III or IVA, Stage IVB, or Recurrent Endometrial Cancer

→ Central Testing for Mismatch Repair Status
Trial designed to test efficacy in 2 distinct patient populations proficient & deficient mismatch repair

→ Arm 1: Chemotx + Placebo for 6 cycles followed by maintenance with placebo for up to 29 cycles

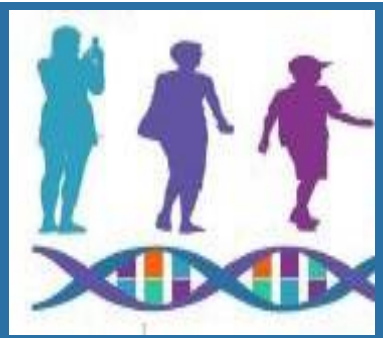
→ Arm 2: Chemotx + pembrolizumab for 6 cycles followed by maintenance w/ pembrolizumab for up to 29 cycles

Pembro with chemotx met its primary endpoint of PFS regardless of mismatch repair status

Major efficacy outcome measure PFS (assessed by investigator per RECIST 1.1). In dMMR cohort, median PFS was not reached (NR) (95% CI: 30.7, NR) in pembrolizumab + chemotx arm and 6.5 months (95% CI: 6.4, 8.7) in placebo & chemothx arm (HR 0.30 [95% CI: 0.19, 0.48]; p-value <0.0001). In pMMR cohort, median PFS was 11.1 months (95% CI: 8.7, 13.5) in pembrolizumab & chemotx arm and 8.5 months (95% CI: 7.2, 8.8) for those receiving placebo and chemotx arm (HR 0.60 [95% CI: 0.46, 0.78; p-value <0.0001).

Key Accomplishment:
Conduct of Collaborative Trials in Special Populations - AYA

S1826: Phase 3 Randomized Study of Nivolumab + AVD or Brentuximab Vedotin + AVD in Patients (Age >/= 12 Years) with Newly Diagnosed Advanced Stage Classical Hodgkin Lymphoma



Study Opened: July 2019
Study Closed: Dec 2022
994 Patients Enrolled (M/F: 45% vs 55%)

- **12 – 17 yrs: 24%**
- **18 – 60 yrs: 66%**
- **Over 60 yrs: 10%**

White 76%, Black, 12%, Asian 3%; Hispanic 13%

Results Presented 2023 ASCO Plenary Session

J Clin Oncol 41, 2023 (suppl 17; abstr LBA4)

- N-AVD improved progression-free survival (PFS) compared to Bv-AVD as initial treatment of advanced stage cHL
- N-AVD was well-tolerated
  - Few immune-related adverse events
  - < 1% of patients received radiation therapy (RT)
- Key step towards harmonizing pediatric and adult therapy of cHL
- **N-AVD is poised to be a new standard for treatment of advanced stage cHL**

Pragmatica-Lung Phase 3 Trial: Streamlined Model for Future Cancer Clinical Trials

Part of a broad effort by NIH/NCI & FDA to modernize IND trials. Pragmatic Clinical Trials with fewer & simpler eligibility criteria than conventional trials (while still ensuring safety of patients):

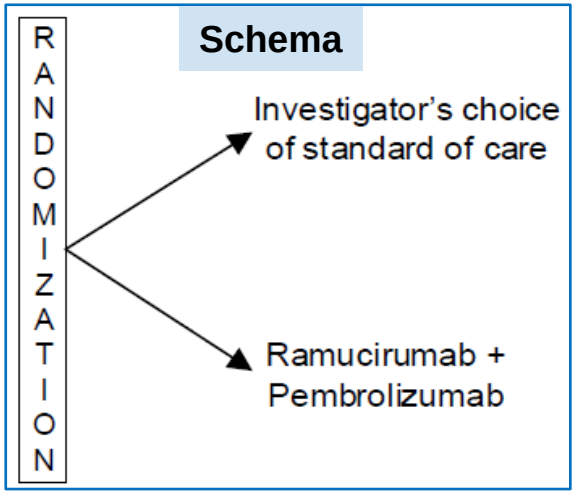
- ❑ Less burdensome to patients and investigators
- ❑ Accrue study participants faster
- ❑ More representative of real-world patient population
- ❑ Serve as a model for future cancer clinical trials

Trial Development Time:
~ 200 days

Initial Total Target Sample Size:
700 pts
(amendment to increase to 800)

Activated: March 6, 2023

Enrollment as of 8/23/2024:
612 pts (87%) of initial sample size
& (77%) of new target of 800 pts



Patient Race	Trial %	SEER % at Dx
> 1 Race	0.8%	
Not Reported	3.4%	
American Indian/ Alaskan Native	0.6%	0.4%
Asian & Native Hawaiian/Pacific Islander	4.6%	4.0%
Black/African American	14.5%	10.8%
White	76.0%	84.8%

Based on enrollments as of 5/31/2024 & Census-adjusted SEER incidence rates 2017-2021 dx years

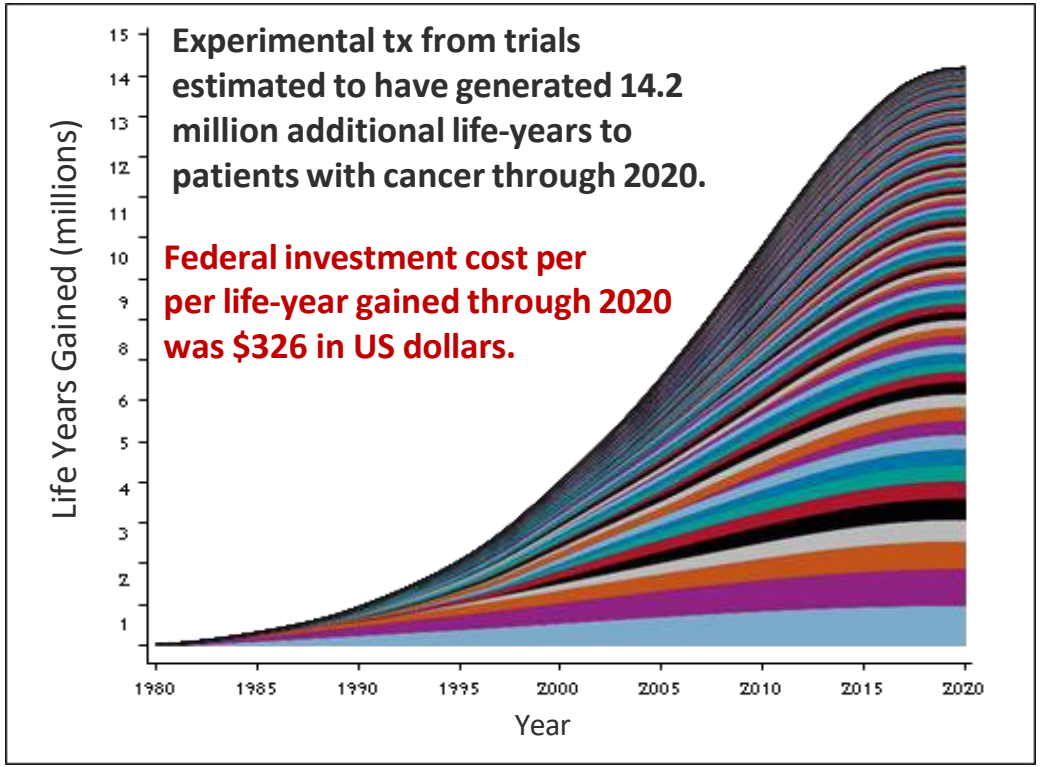
Population, Clinical, and Scientific Impact of National Cancer Institute's National Clinical Trials Network Treatment Studies

Unger JM et al, JCO, 2023 Apr 10;41(11):2020-2028. doi: 10.1200/JCO.22.01826. Epub 2022 Dec 8.

162 Adult NCTN positive, randomized trials since 1980 analyzed comprising 108,334 patients. Trials cited 165,336 times thru 2020, with 87.7% cited in cancer care guidelines favoring recommended tx.

Relevance: Impact of US NCTN trials on adult cancer outcomes cannot be overstated; this evidence should compel sustained financial investment and continued academic contributions to this valuable resource.*

*Relevance section written by *JCO* Editor-in-Chief Jonathan W. Friedberg, MD.



Cumulative life-years gained through 2020 by Study

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