Eliminating Disparities in Access to Quality Care in Patients With Gastric and Esophagogastric Junction Adenocarcinoma

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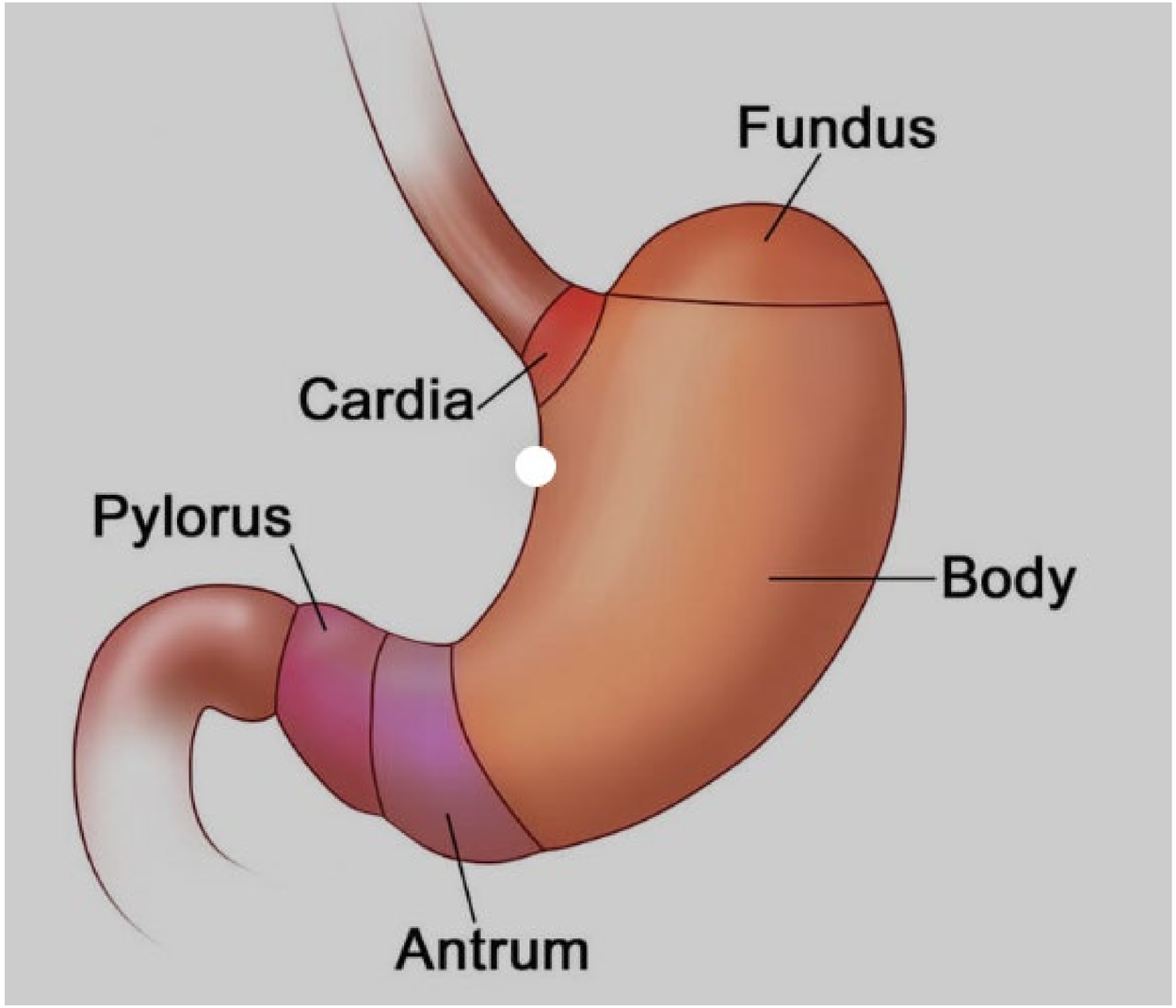
DISCLOSURES:

- Tomislav Dragovich has no financial relationships with commercial interests
- Tonya J. Kinsinger has no financial relationships with commercial interests to disclose.

Changing epidemiology and pathophysiology of GEJ and gastric cancer in the US



Gastric and GEJ cancer: Risk Factors

- H. Pylori
- GERD
- Barrett's esophagus
- Obesity
- Tobacco (SCC)
- ETOH (SCC)

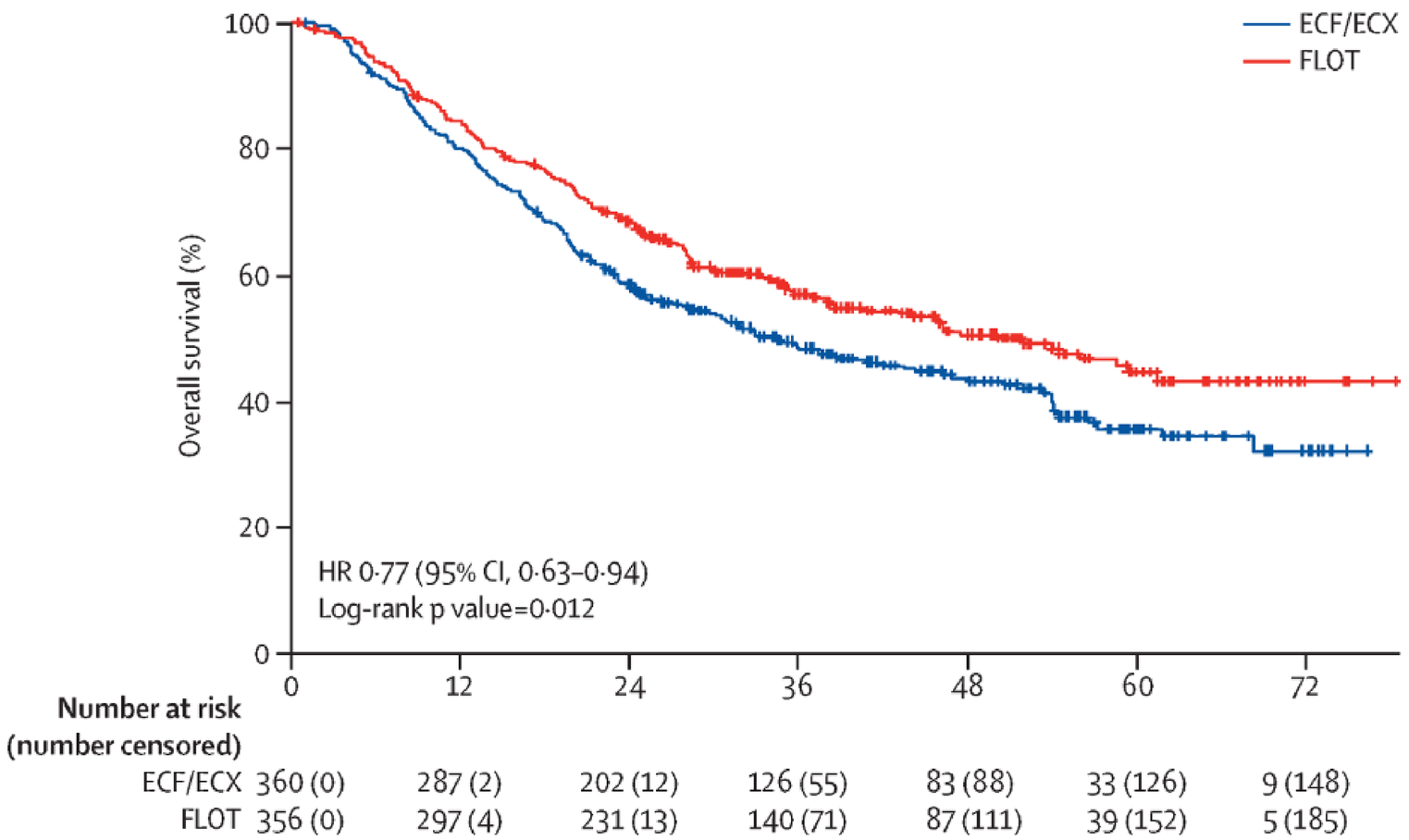
Treatment landscape in 2022 in the US

- Multidisciplinary approach
- Increasing utilization of perioperative (neoadjuvant chemotherapy)
- Increasing use of targeted therapy and immunotherapy

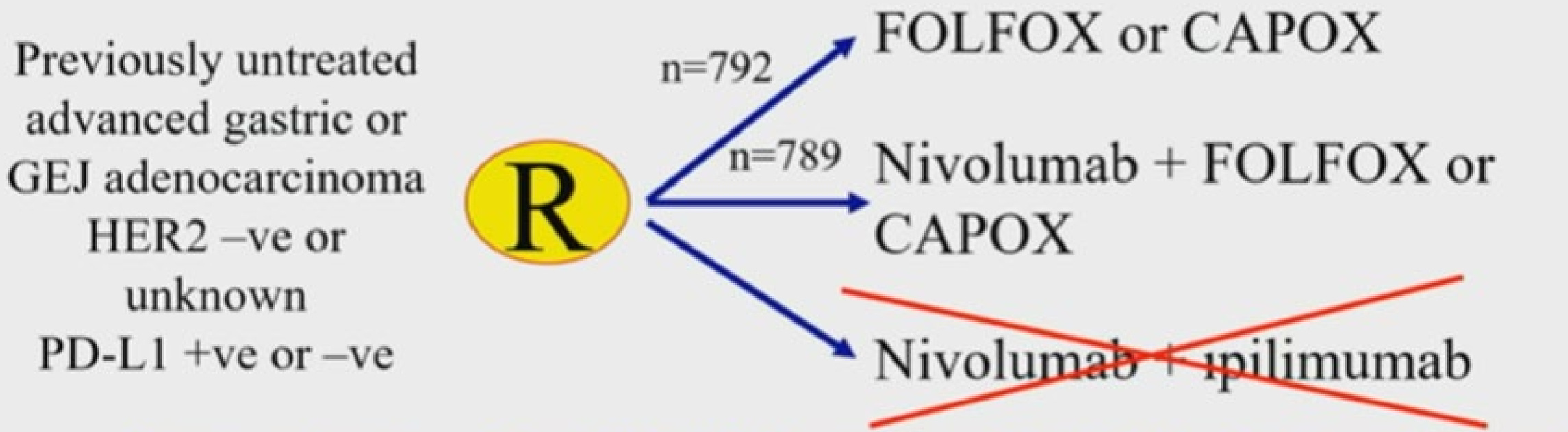
Stage-based survival in the US

SEER stage	5-year relative survival rate
Localized	70%
Regional	32%
Distant	6%
All SEER stages combined	32%

Perioperative Therapy (Neoadjuvant)



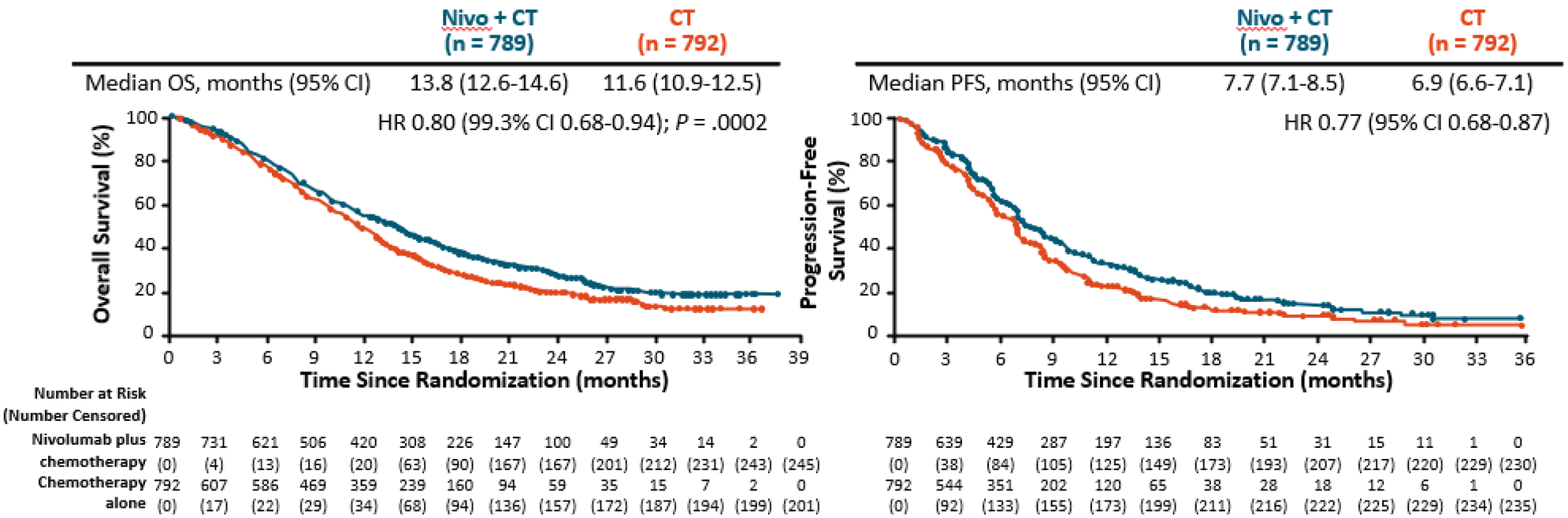
Randomised first line phase III nivolumab study in gastric and GEJ adenocarcinoma (CHECKMATE-649)



Primary endpoint: OS and PFS (PD-L1 expression CPS ≥5; Dako 28-8 pharmDx assay)

Janjigian et al, Lancet, 2021

CheckMate 649: Overall OS and PFS

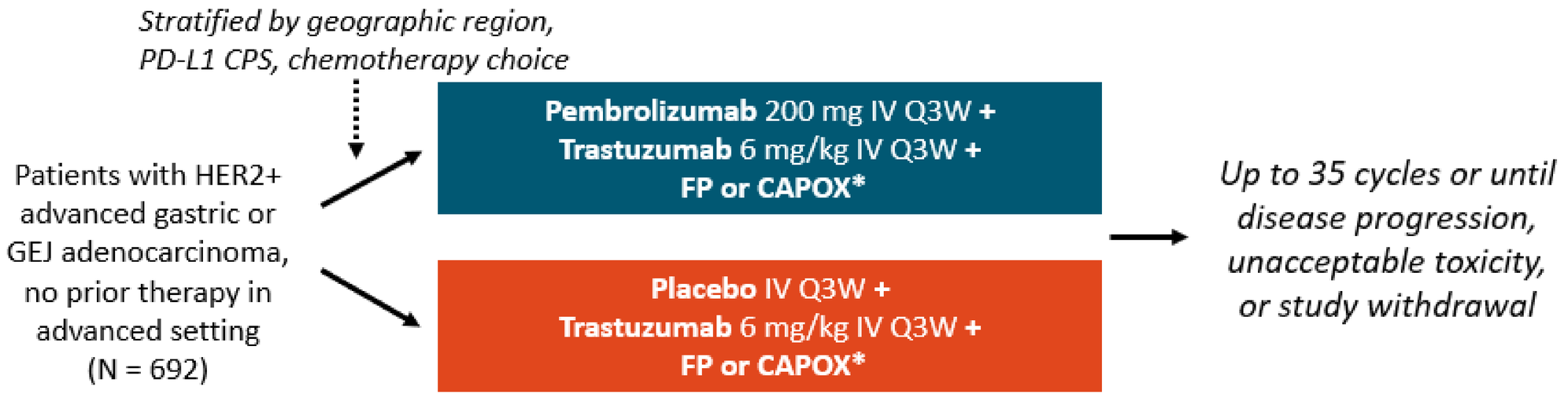


- Minimum follow-up: 12.1 mo
- Nivolumab + CT increased OS vs CT in most prespecified subgroups

Janjigian et al, Lancet, 2021

KEYNOTE-811 Interim Analysis: Study Design

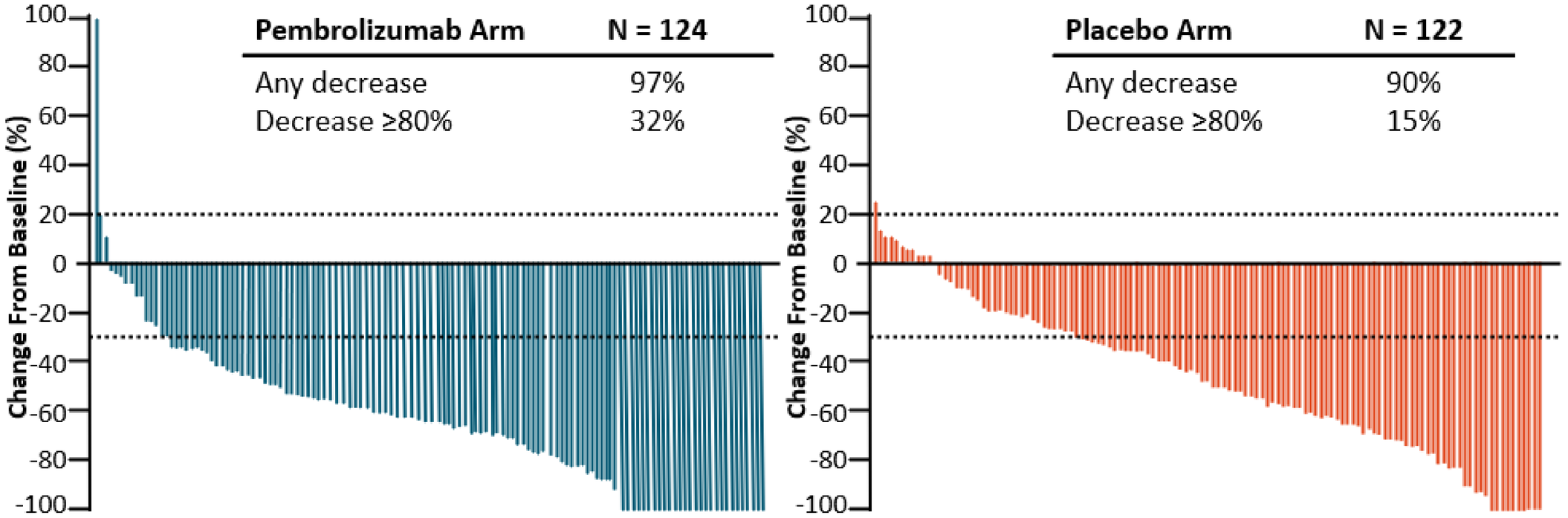
- Randomized, double-blind, placebo-controlled phase III study



*Trastuzumab 8 mg/kg loading dose.
FP: 5-fluorouracil 800 mg/m² IV Days 1-5 Q3W + cisplatin 80 mg/m² IV Q3W.
CAPOX: capecitabine 1000 mg/m² BID Days 1-14 Q3W + oxaliplatin 130 mg/m² IV Q3W.

- Efficacy analysis: first 264 patients enrolled; safety analysis: 433 patients who received ≥1 dose of study medication
- **Primary endpoints:** OS, PFS per RECIST v1.1 by BICR

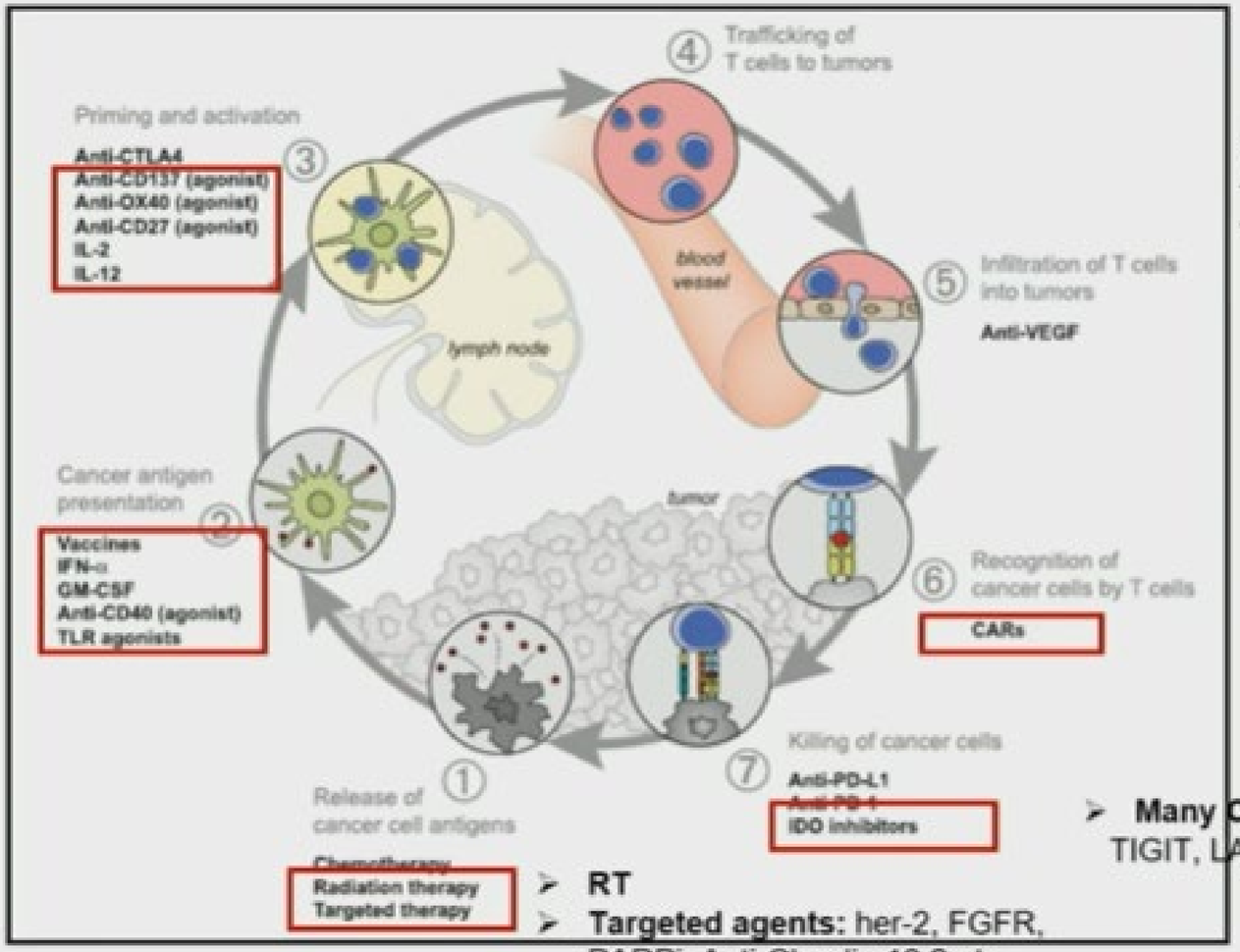
KEYNOTE-811 Interim Analysis: Target Lesion Change From Baseline



Expanding our armamentarium for the treatment of gastric cancer

- **Many agonists**
  GITR, 4-1BB, OX 40, IL-2 etc

- **Vaccines**
- **Neoantigen specific immunotherapy: targeting her-2**
- **Oncolytic virus: Telomelysin**



- **TGF-b in TME suppression**
  - Vactosertib
  - M7824 (bispecific inhibitors of TGF-b and PD-L1)

- **CAR-T cells targeting**
  her-2, cluadin 18.2, MUC etc..

- **Many Co-inhibitory molecules:**
  TIGIT, LAG-3, TIM-3 etc..

- **RT**
- **Targeted agents:** her-2, FGFR, PARPi, Anti-Cluadin 18.2 etc

…But… are these improvements reaching all communities?

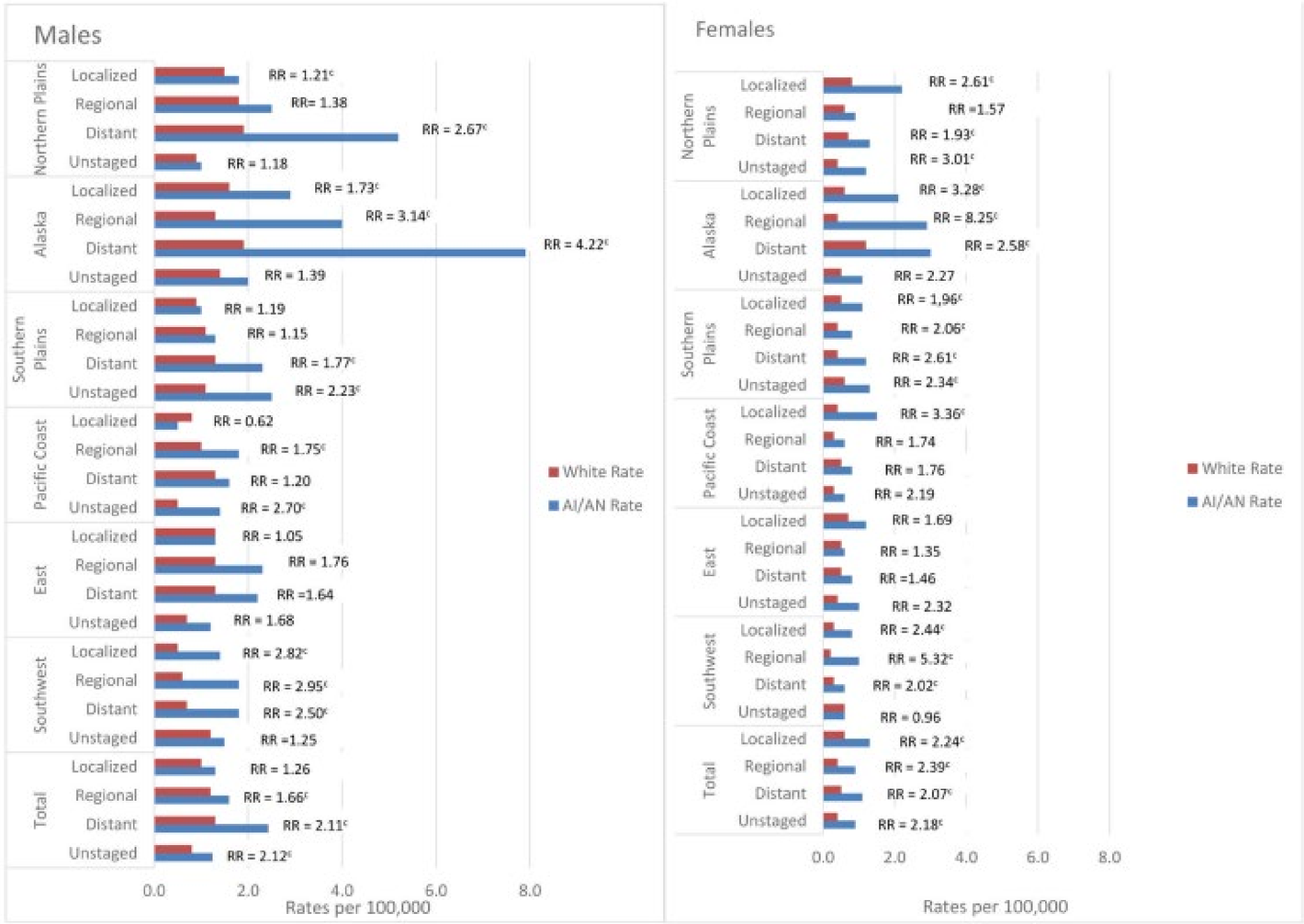
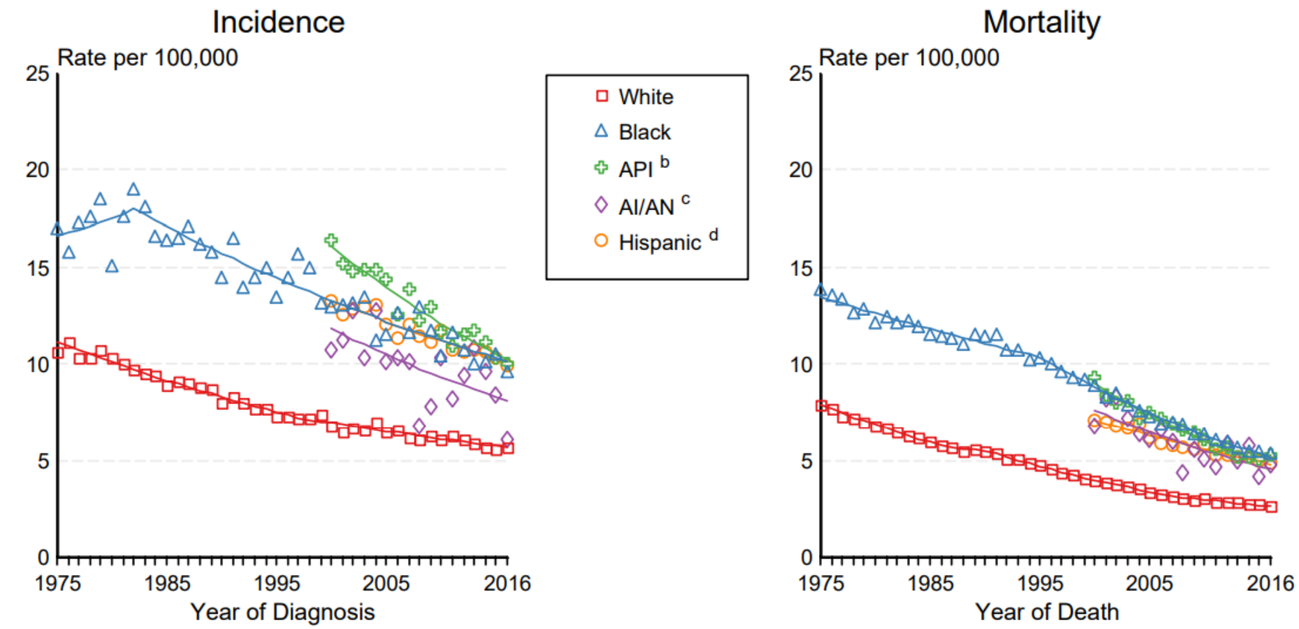


Figure 1:
Gastric cancer incidence rates[a] and rate ratios by stage of diagnosis, sex, and Indian Health Service region for American Indian/Alaska Native[b] and white populations in PRCDA counties, 2005–2016.

Melconian et al. Am J Gastroenterol. 2020 December ; 115(12): 1989–1997

Incidence, mortality …

SEER Incidence and US Death Rates[a]
Cancer of the Stomach, Both Sexes
Joinpoint Analyses for Whites and Blacks from 1975-2016
and for Asian/Pacific Islanders, American Indians/Alaska Natives and Hispanics from 2000-2016



Source: Incidence data for whites and blacks are from the SEER 9 areas (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, Atlanta).
Incidence data for Asian/Pacific Islanders, American Indians/Alaska Natives and Hispanics are from the SEER 21 areas (SEER 9 areas, San Jose-Monterey, Los Angeles, Alaska Native Registry, Rural Georgia, California excluding SF/SJM/LA, Kentucky, Louisiana, New Jersey, Georgia excluding ATL/RG, Idaho, New York and Massachusetts).
Mortality data are from US Mortality Files, National Center for Health Statistics, CDC.

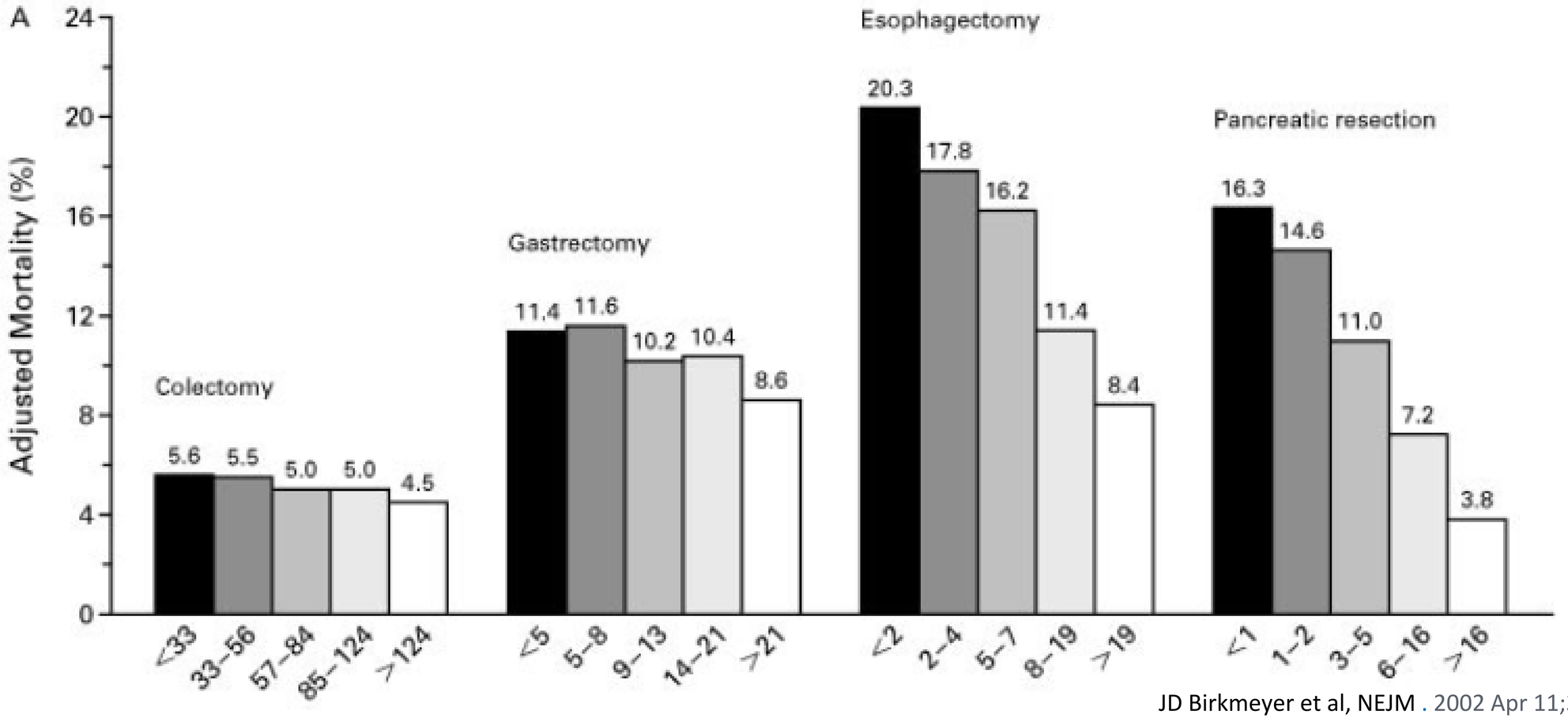
[a] Rates are age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1103).
Regression lines are calculated using the Joinpoint Regression Program Version 4.7, February 2019, National Cancer Institute. Joinpoint analyses for Whites and Blacks during the 1975-2016 period allow a maximum of 5 joinpoints. Analyses for other ethnic groups during the period 2000-2016 allow a maximum of 3 joinpoints.

[b] API = Asian/Pacific Islander.

[c] AI/AN = American Indian/Alaska Native. Rates for American Indian/Alaska Native are based on the Purchased/Referred Care Delivery Area (PRCDA) counties.

[d] Hispanic is not mutually exclusive from whites, blacks, Asian/Pacific Islanders, and American Indians/Alaska Natives. Incidence data for Hispanics are based on NHIA and exclude cases from the Alaska Native Registry.

Adjusted In-Hospital or 30-Day Mortality among Medicare Patients (1994 through 1999), According to Quintile of Total Hospital Volume for Resections of Gastrointestinal Cancer (Panel A)



JD Birkmeyer et al, NEJM . 2002 Apr 11;346(15):1128-37.

True or False?

- “The best management for any cancer patient is in a clinical trial”

- Yet, only 2-7% of all cancer patients end up participating in clinical trials

Clinical Trial Barriers

"It is rational to try to enroll a population that is more representative of the actual population that will benefit from the treatment and so we try to think carefully about the inclusion/exclusion criteria. That also has the added benefit for us of reducing cost because we are reducing the number of patients we have to screen."

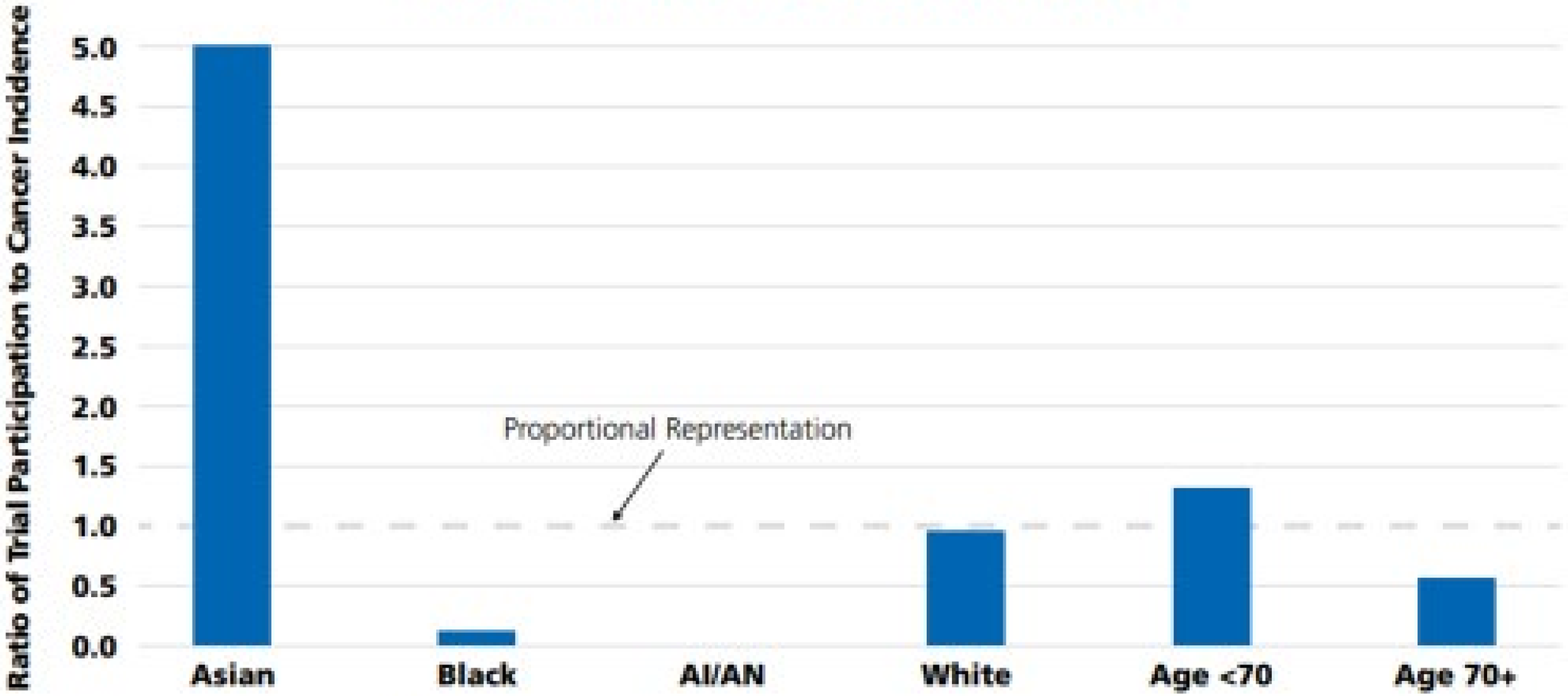
— Joanne Lager, MD, Head, Oncology Development, Sanofi

Diversity/Inclusion

- Response to drugs can differ based on factors such as sex, ethnicity and socio-economic factors
- ACCESS: more than 70% of cancer patients receive treatment in community setting)
- Adequate representation of all demographic groups (if results of the trial to be applicable to general population)

Carpten JD et al, Nature Reviews, Cancer, Vol 21, Oct 2021

DEMOGRAPHIC REPRESENTATION IN FDA-SUBMITTED CANCER TRIALS



Sources: Singh (2017) FDA analysis of enrollment of older adults in clinical trials for cancer drug registration: A 10-year experience by the U.S. Food and Drug Administration, ASCO Annual Meeting. FDA cancer trials 2005-2015; Fashoyin-Aje (2017), Racial composition in trials supporting the U.S. approval of anti-cancer new molecular entities (NMEs): 2011- 2016. ASCO Annual Meeting

AI/AN = American Indian/Alaska Native

Diversity/Inclusion

- Eliminate burdensome requirements that may alienate certain segments of population or discriminate against old age, gender minorities, patients with co-morbidities

- COVID 19 pandemic provided a platform to “pressure test” some of the new approaches (virtual consenting, de-centralized and simplifying study procedures).

CASE STUDY # 1

Mr. Jones is a 78 y/o Hispanic male with locally advanced adenocarcinoma of the esophagogastric junction.

- He is currently receiving FOLFOX every 14 days.
- He reports having uncontrolled nausea and vomiting for ten days after his first cycle of FOLFOX.
- He denies filling his prescriptions for his oral antiemetics because he limited finances (fixed income) to pay his copays for his medications.
- Today is Cycle # 2, Day 1.

NAUSEA & VOMITING

5-HT3 RECEPTOR ANTAGONISTS:

- ONDANESTRON
- DOLASETRON
- GRANISTETRON

NCCN Guidelines Version 2.2022 Antiemesis

NAUSEA & VOMITING

PHENOTHIAZINES:

- PROCHLORPERAZINE
- PROMETHAZINE

CORTICOSTEROIDS:

- DEXAMETHASONE

NCCN GUIDELINES VERSION 2.2022 ANTIEMESIS

NAUSEA & VOMITING

ATYPICAL ANTIPSYCHOTIC:
- OLANZAPINE

BENZODIAZIPINE:
- LORAZEPAM

CANNABINOID:
- DRONABINOL

OTHER:
- SCOPOLAMINE PATCH

NCCN GUIDELINES VERSION 2.2022 ANTIEMESIS

NAUSEA & VOMITING

Prescribe H2 blocker or proton pump inhibitor for patient.

- Dyspepsia can mimic nausea.

Medications:

- Famotidine
- Omeprazole
- Pantoprazole
- Esomeprazole

NCCN GUIDELINES VERSION 2.2022 ANTIEMESIS

NAUSEA AND VOMITING:

LIFESTYLE CHANGES:

- Eating six to eight small meals per day.
- Do not skip meals.
- Choosing healthy foods.
- Avoid foods with strong odors.
- Eating foods at room temperature.
- Nutrition consult.

National Cancer Institute: Eating Hints: Before, During, and After Cancer Treatments. .

TRANSPORTATION:

- A patient may have transportation benefits if they have AHCCCS.
- American Cancer Society: Road to Recovery.
- Area Agency on Aging: Elderlyft (Maricopa county only).
- Valley Metro (dial a ride).

CASE STUDY # 2:

Ms. Smith is a 42 y/o Native American with gastric cancer. She is currently receiving FLOT every 14 days.

- She reports having diarrhea since her last chemo. She reports having more than six watery stools per day.
- She reports minimal improvement in her diarrhea with one Loperamide QID as needed.
- She denies having running water or electricity at home.
- Today is Cycle # 4, Day 1.

DIARRHEA

Evaluate patient's stool for possible infectious causes:

- Clostridium Difficile
- Stool culture with Shiga toxin
- Fecal leukocytes
- Ova and parasites

DIARRHEA

- LOPERAMIDE
- DIPHENOXYLATE/ATROPINE
- TINCTURE OF OPIUM

DIARRHEA

LIFESTYLE CHANGES:

- Use flushable toilet wipes as needed after defecation.
- Apply topical cream externally to perirectal area as needed.
- Use hand sanitizer.

DIARRHEA:

LIFESTYLE CHANGES:

- Increase your daily intake of oral fluids to prevent dehydration. Goal: 64 ounces of noncaffeinated beverages.
- Follow the BRAT (bananas, rice, applesauce, and toast) diet until your diarrhea decreases.
- Limit your intake of dairy products (except yogurt) until your diarrhea decreases

INFECTION PREVENTION:

National Comprehensive Cancer Network:

- Does not recommend antimicrobial prophylaxis for bacterial infections for standard chemotherapy regimens for most solid tumors.
- Anticipated neutropenia less than seven days.

Patient education:

- Good hand hygiene.
- Call the office or go to the ER if you develop a temperature greater than 100.4.

CASE STUDY # 3:

Mr. Miller is 56 y/o African American male with esophagogastric junction adenocarcinoma with liver metastases. He is currently receiving Paclitaxel IV on day 1, 8, and 15 with Ramucirumab IV on day 1 and 15 every 28 days.

- He reports increased abdominal pain and increased abdominal bloating.
- He reports increased bilateral lower extremity edema.
- He reports reports decreased appetite and early satiety.
- He reports intermittent constipation.
- Today is Cycle # 4, Day 1.

PAIN

Complete comprehensive pain assessment on patient:

- Pain experience
- List of potential risk factors for misuse/abuse
- Psychosocial support
- Medical history
- Clinical assessment, physical examination, labs, and imaging studies to evaluate for disease progression

NCCN GUIDELINES VERSION 2.2022 Adult Cancer Pain

PAIN

Non-opioid analgesic:

- Acetaminophen
- Nonsteroidal anti-inflammatory drugs

Adjuvant analgesics for neuropathic pain:

- Antidepressants
- Anticonvulsants
- Topical agents
- Corticosteroids

NCCN GUIDELINES VERSION 2.2022 Adult Cancer Pain

PAIN

Opioids:

- Morphine sulfate
- Hydromorphone
- Fentanyl
- Methadone
- Oxycodone
- Hydrocodone
- Oxymorphone
- Tramadol
- Codeine
- Tapentadol

NCCN GUIDELINES VERSION 2.2022 Adult Cancer Pain

CONSTIPATION:

- Evaluate patient for bowel obstruction.

Medications:

- Polyethylene glycol
- Sennosides-Docusate sodium tablets
- Lactulose
- Titrate the Polyethylene glycol, Sennosides-Docusate sodium, and Lactulose as needed

ASCITES

- Ultrasound-guided paracentesis.
- Place an abdominal PleurX catheter in patient.
- Educate patient and/or family member on procedure to drain patient's PleurX.
- Instruct patient and/or family member on the frequency to drain patient's PleurX catheter.
- Order supplies for patient.
- Prescribe diuretic for patient.

LOWER EXTREMITY EDEMA

- Evaluate patient for deep venous thrombosis (DVT).
- Elevate lower extremities
- Compression stockings
- Prescribe a diuretic for patient.
- Educate patient

DEEP VENOUS THROMBOSIS AND/OR PULMONAY EMBOLUS

- ENOXAPARIN
- RIVAROXABAN
- APIXABAN

NUTRITION

- Eat six to eight small meals per day.
- Supplement your calories with Ensure, Boost, Carnation Instant Breakfast, Glucerna, or protein shakes daily as needed.
- Consult nutrition.

Disparities in Cancer Care

”Injustice anywhere is threat to justice everywhere”

Martin Luther King Jr.