Clinical Trials in Cervical Cancer – Can they be all we want them to be?

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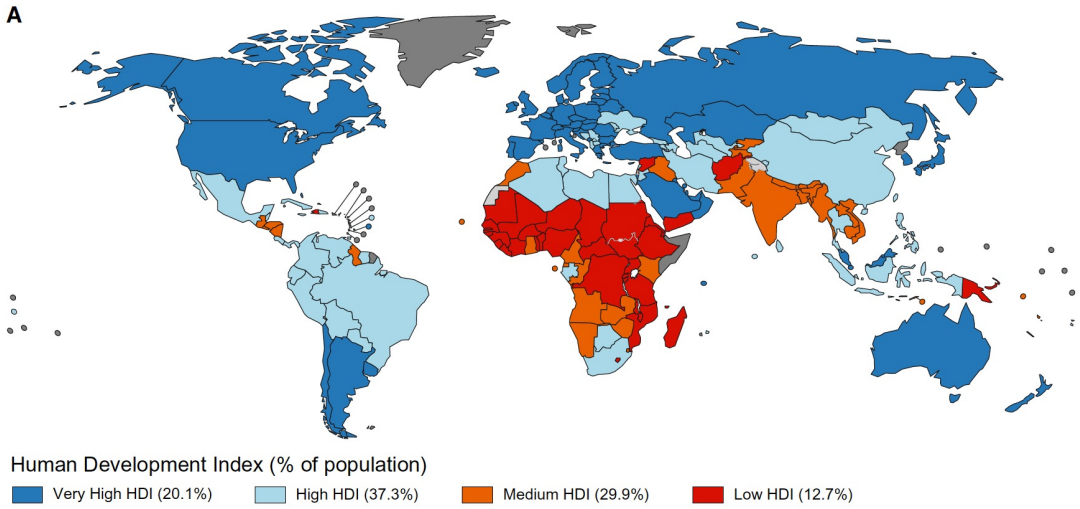
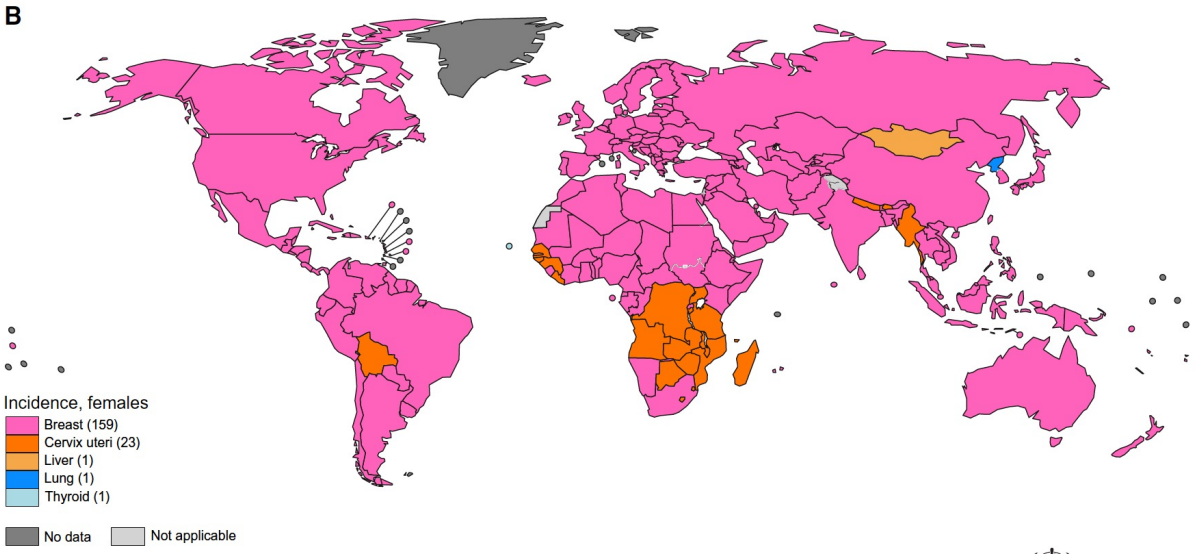
Disclosures

- Grants – NCI - UG1 CA23330, P50 CA 098252
- Contracted Research – Agenus, Seattle Genetics, Rubius Therapeutics
- Scientific Advisory Board – Seattle Genetics

Cervical Cancer – A Global Problem

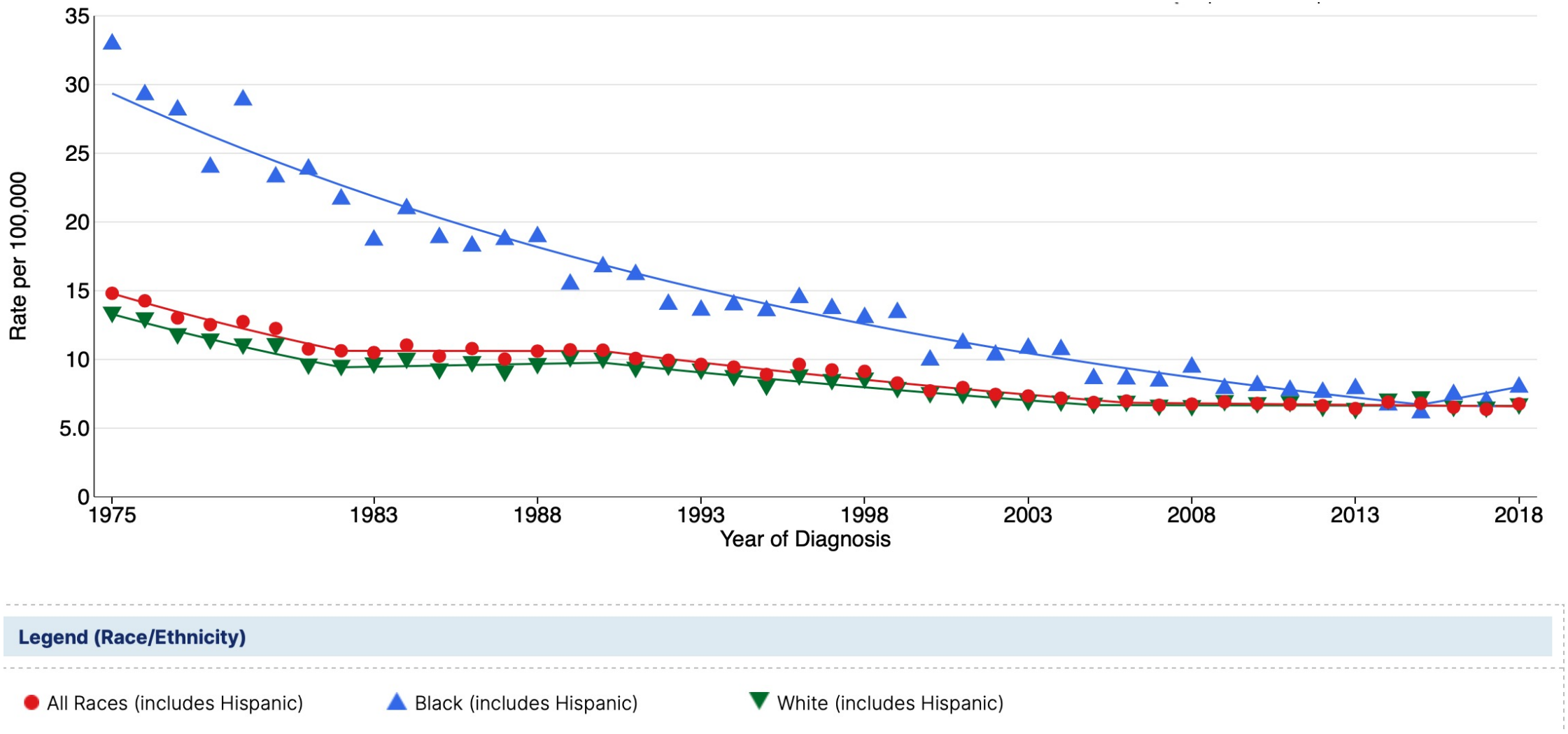
- 604, 127 (3.1%) cases
- 341, 831 (3.4%) deaths





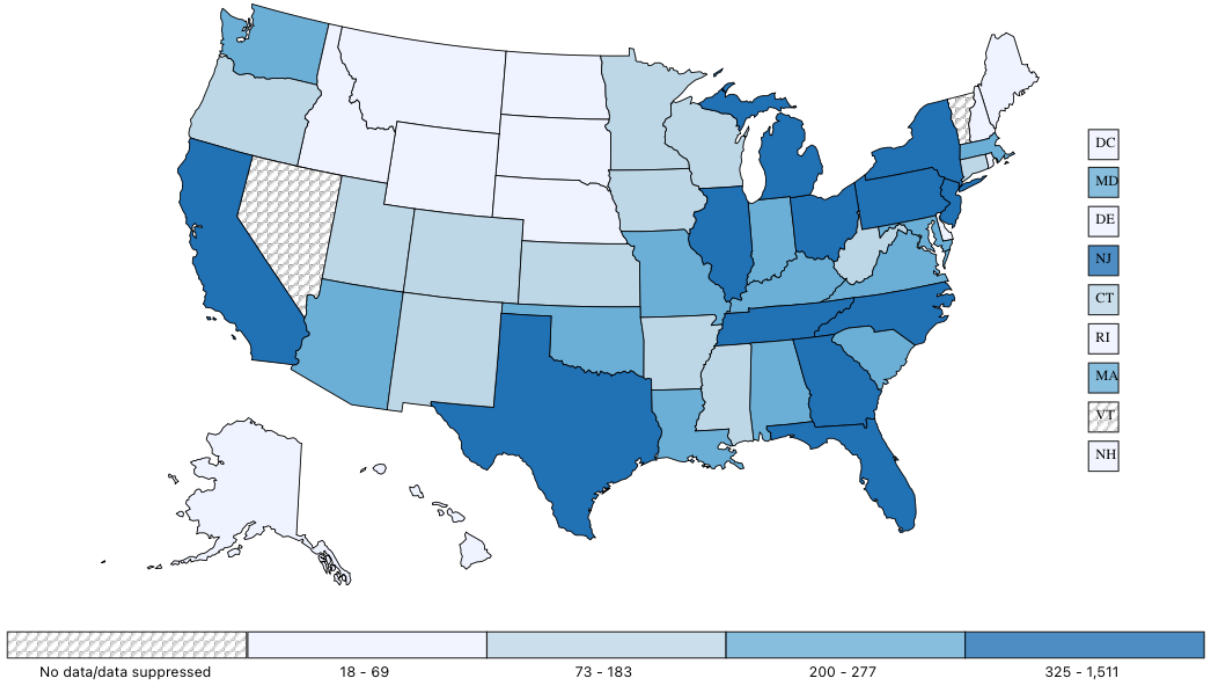
 Sung H et al. *CA Cancer J Clin* 2021

Four Decades of Cervical Cancer in the US – Why we are here today



SEER.Cancer.gov

Access to care – Where are the majority of patients?



Number of New Cancers in the United States, 2018
Cervix, All Ages, All Races and Ethnicities, Female

NCI Designated Comprehensive Centers / NCCN Sites

6 Cancer.gov, NCCN.org

Locally Advanced Cervical Cancer

- Whole pelvic radiation and brachytherapy was the standard of care
- Then 1999 came along….
- FIVE Practice changing publications referenced by the FDA
  GOG 85 (SWOG 8695), GOG 109 (SWOG/RTOG), GOG 120, GOG 123, and RTOG 90-01

NCI Urges Chemo-RT Combination for Invasive Cervical Cancer

March 31, 1999

Oncology NEWS International, Oncology NEWS International Vol 8 No 4, Volume 8, Issue 4

BETHESDA, Md-The National Cancer Institute (NCI) has recommended that oncologists use a combination of chemotherapy and radiation instead of radiation alone to treat invasive cervical cancer.

Again, how often does this happen?

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NCCN Cervical Cancer Guidelines – NCI Investment

Clinical Stage (CERV-1)
Stage IA1 (no LVSI), Stage IA1 (with LVSI) and Stage IA2, Stage IB1 and Select IB2 (Fertility Sparing) (CERV-2) GOG 278*
Stage IA1 (no LVSI), Stage IA1 (with LVSI) and Stage IA2 (Non-Fertility Sparing) (CERV-3)
Stage IB1, IB2 and Stage IIA1 (Non-Fertility Sparing) (CERV-4) GOG 92, 109 → 263*, 274*
Stage IB3 and Stage IIA2 (Non-Fertility Sparing) (CERV-4) GOG 85, 120, 123, 165, 191,
Stage IB3, Stage IIA2, and Stages IIB, III, and IVA (CERV-6) 219, 9929, GY006*, GY017*
Incidental Finding of Invasive Cancer After Simple Hysterectomy (CERV-9)
Surveillance (CERV-10)
Local/Regional Recurrence (CERV-11)
Stage IVB or Distant Metastases (CERV-12) GOG 43, 110, 149, 169, 179, 204, 240, 265

Principles of Pathology (CERV-A) GOG 49
Principles of Imaging (CERV-B) GOG 233
Principles of Evaluation and Surgical Staging (CERV-C)
Principles of Radiation Therapy (CERV-D)
Sedlis Criteria for External Pelvic Radiation After Radical Hysterectomy In Node-Negative, Margin-Negative, Parametria-Negative Cases (CERV-E)
Systemic Therapy Regimens for Cervical Cancer (CERV-F)

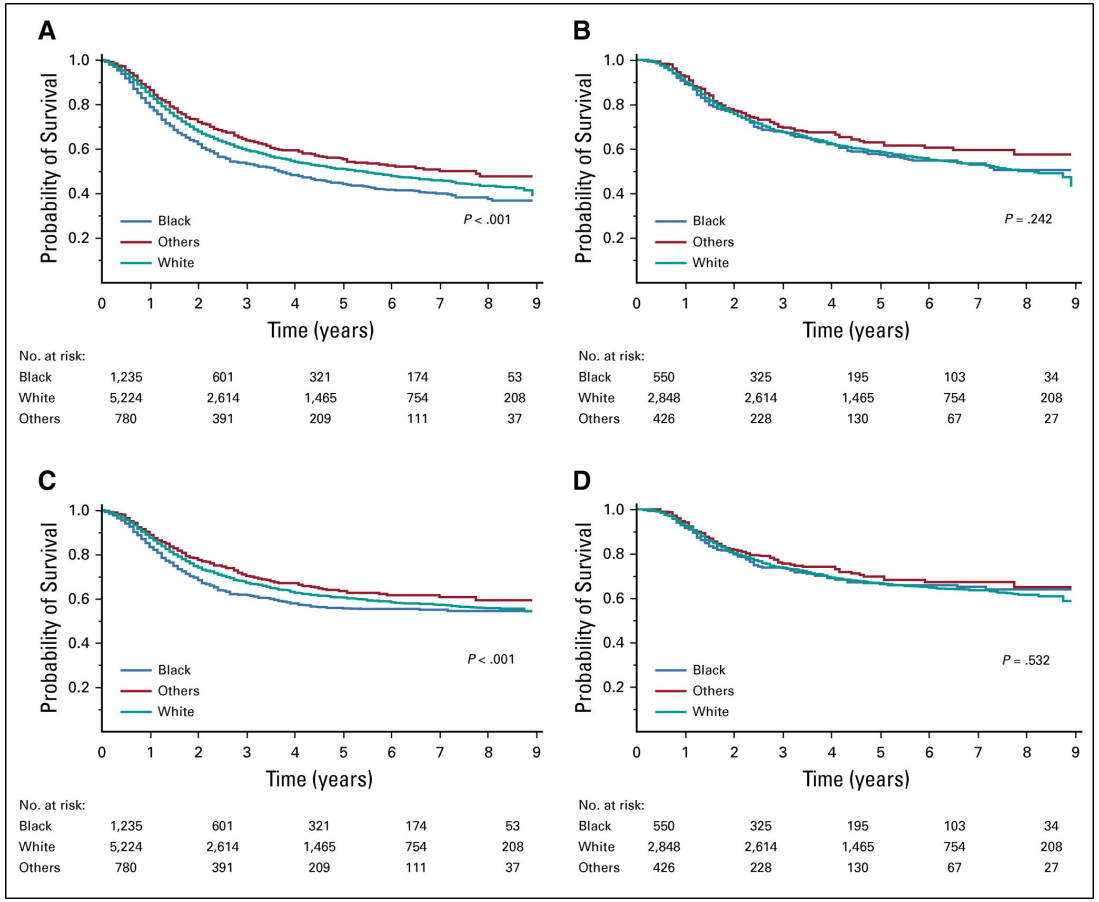
Staging (ST-1)

*Ongoing

Abu-Rustum NR et al. *J Natl Compr Canc Netw* 2020

Receipt of Guideline Adherent Care – 2021

- 52.7% of ALL patients received standard of care treatment for LACC (SEER 2007-2015)
  - Older age, public insurance, and Black race were associated with decreased rates of brachytherapy
- When comparing Black and White patients 5-year OS was 44.2% vs. 50.9% (p <0.0001)
- In patients whose received brachytherapy there was no survival difference

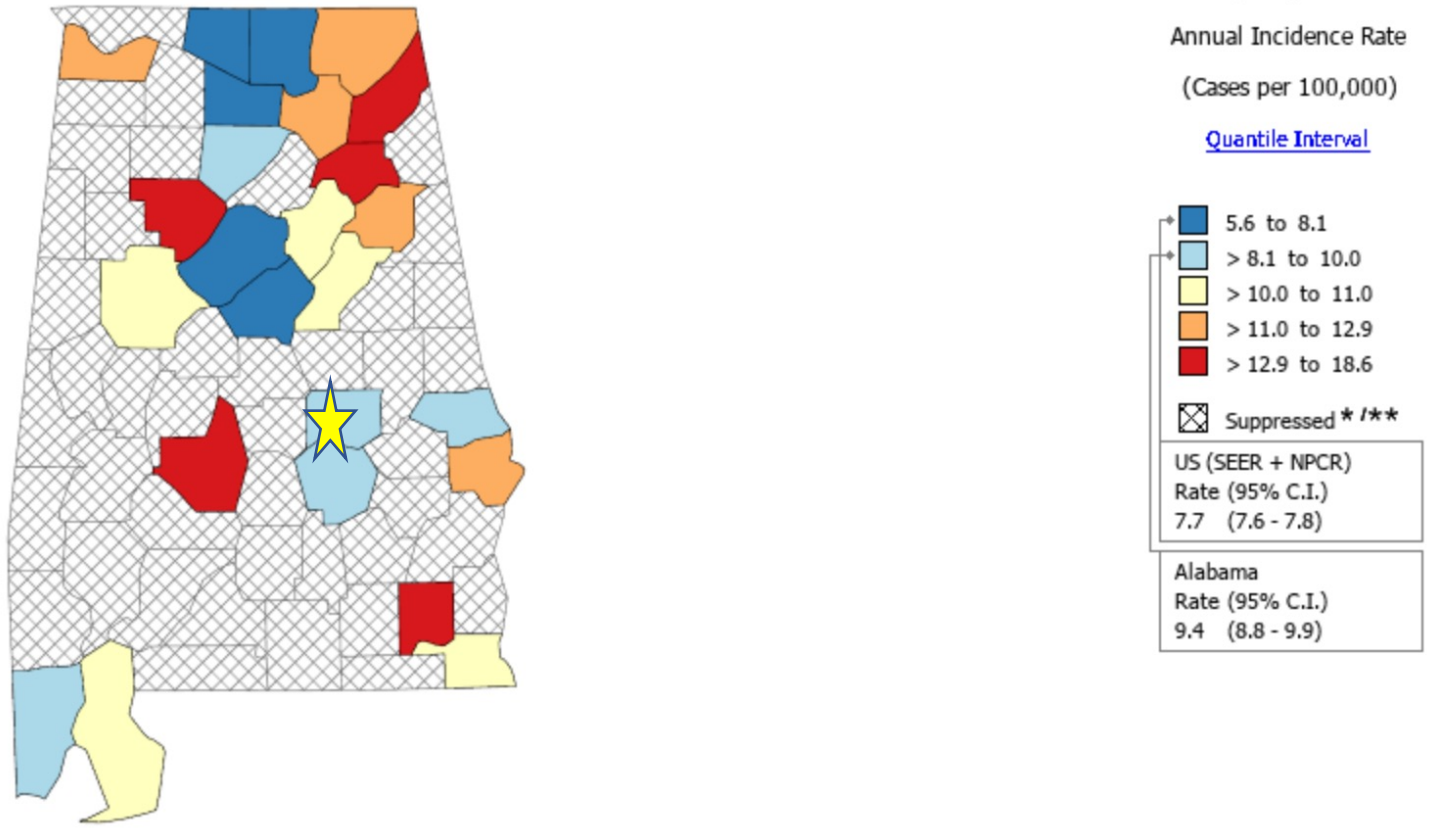


 Boyce-Fappiano D et al. *JCO Oncology Practice* 2021

Observations on Cervical Cancer in Alabama

Cervical Cancer in Alabama

Incidence Rates† for Alabama by County
Cervix, 2014 - 2018
All Races (includes Hispanic), Female, All Ages



Highest incidence counties
1. Dekalb 13.1 (NE)
2. Dale 15.1 (SE)
3. Etowah 15.6 (NE)
4. Walker 15.6 (UCen)
5. Dallas 18.6 (LCen)

 Https://www.statecancerprofiles.cancer.gov

Does distance from a CCC Matter?

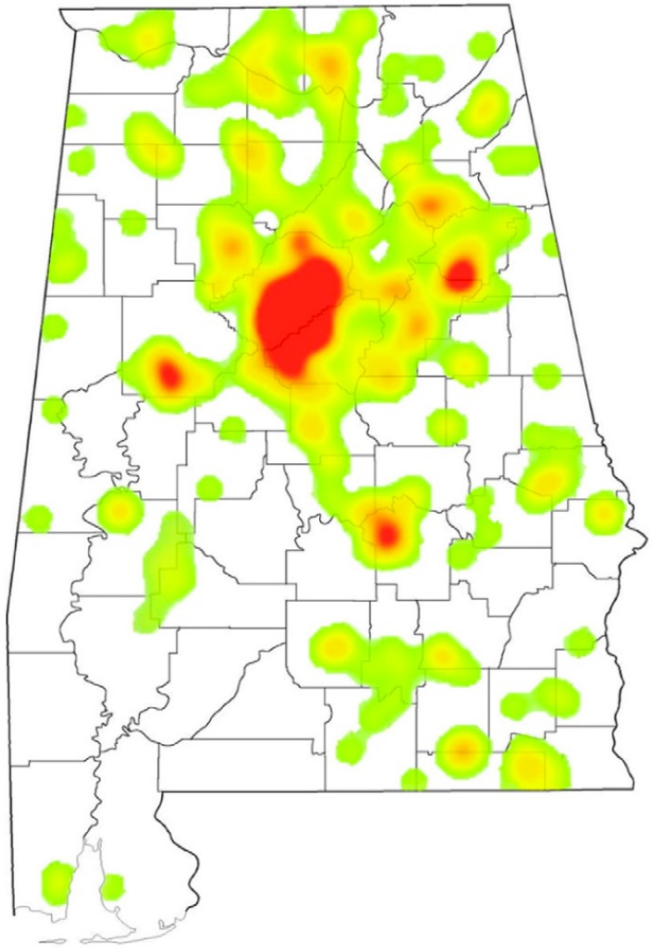
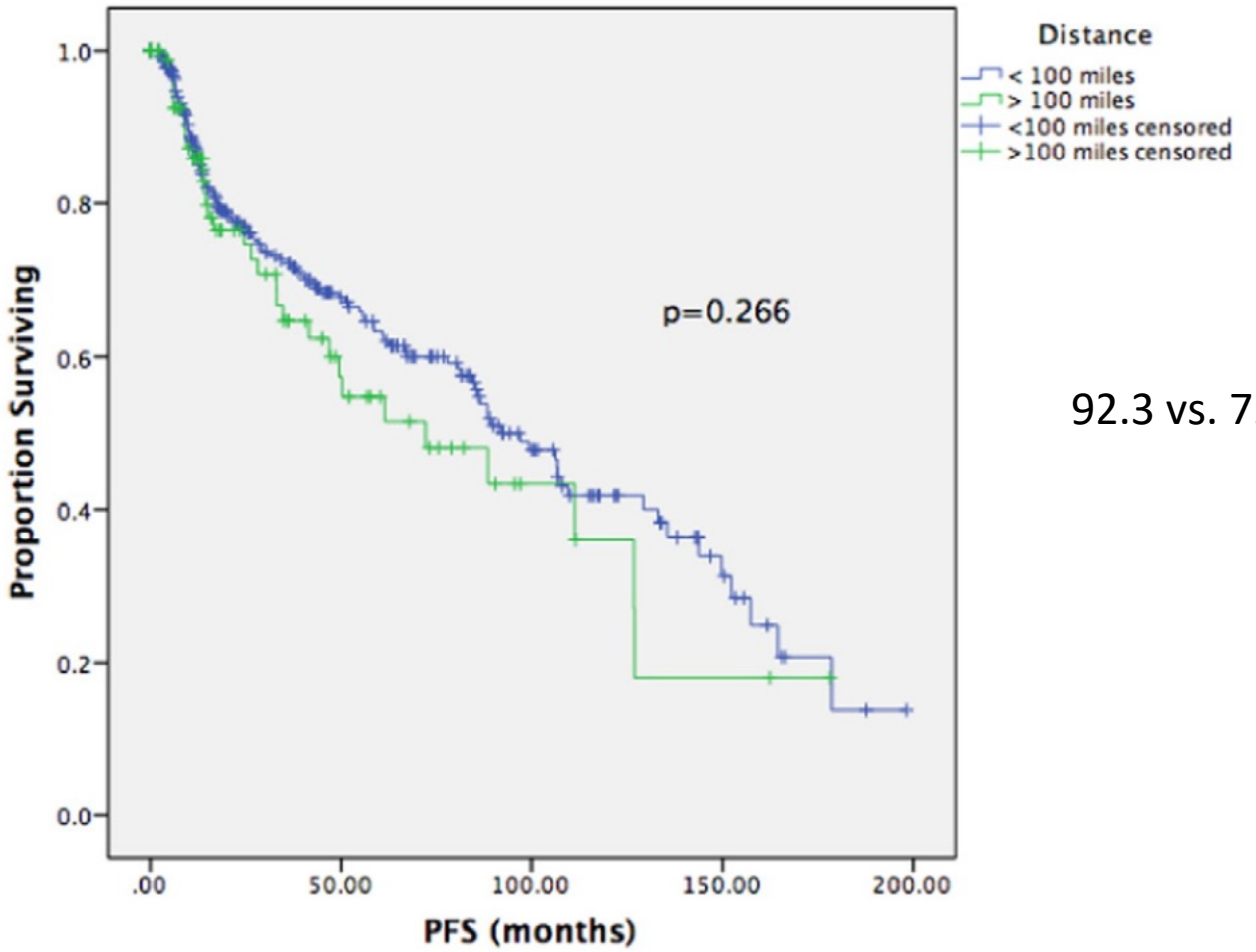


Fig. 1. Geographic distribution heat map of patient residences.



92.3 vs. 72.1 mos

 Barrington DA et al. *Gynecol Oncol* 2016

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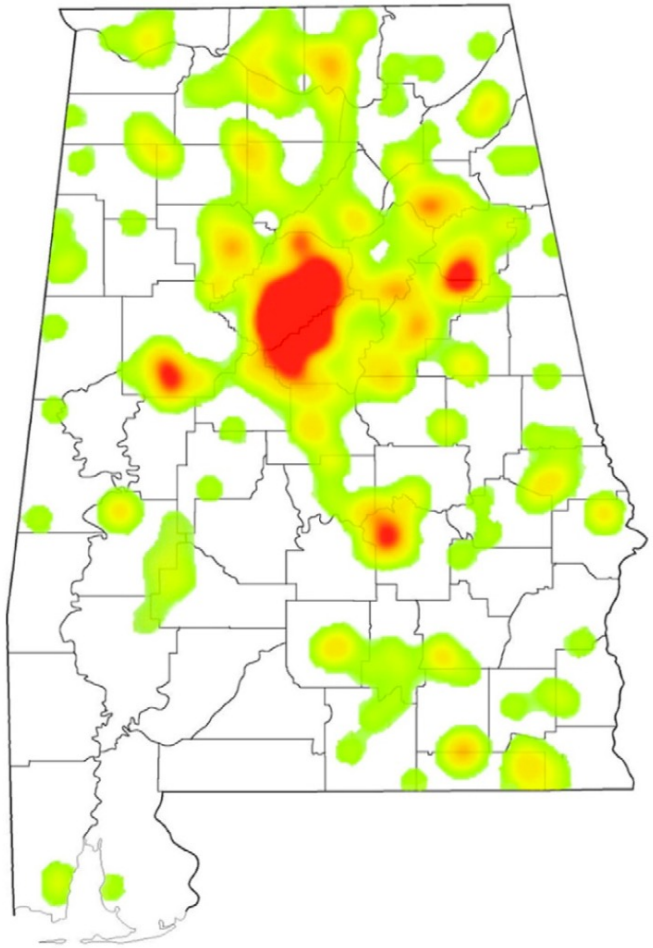

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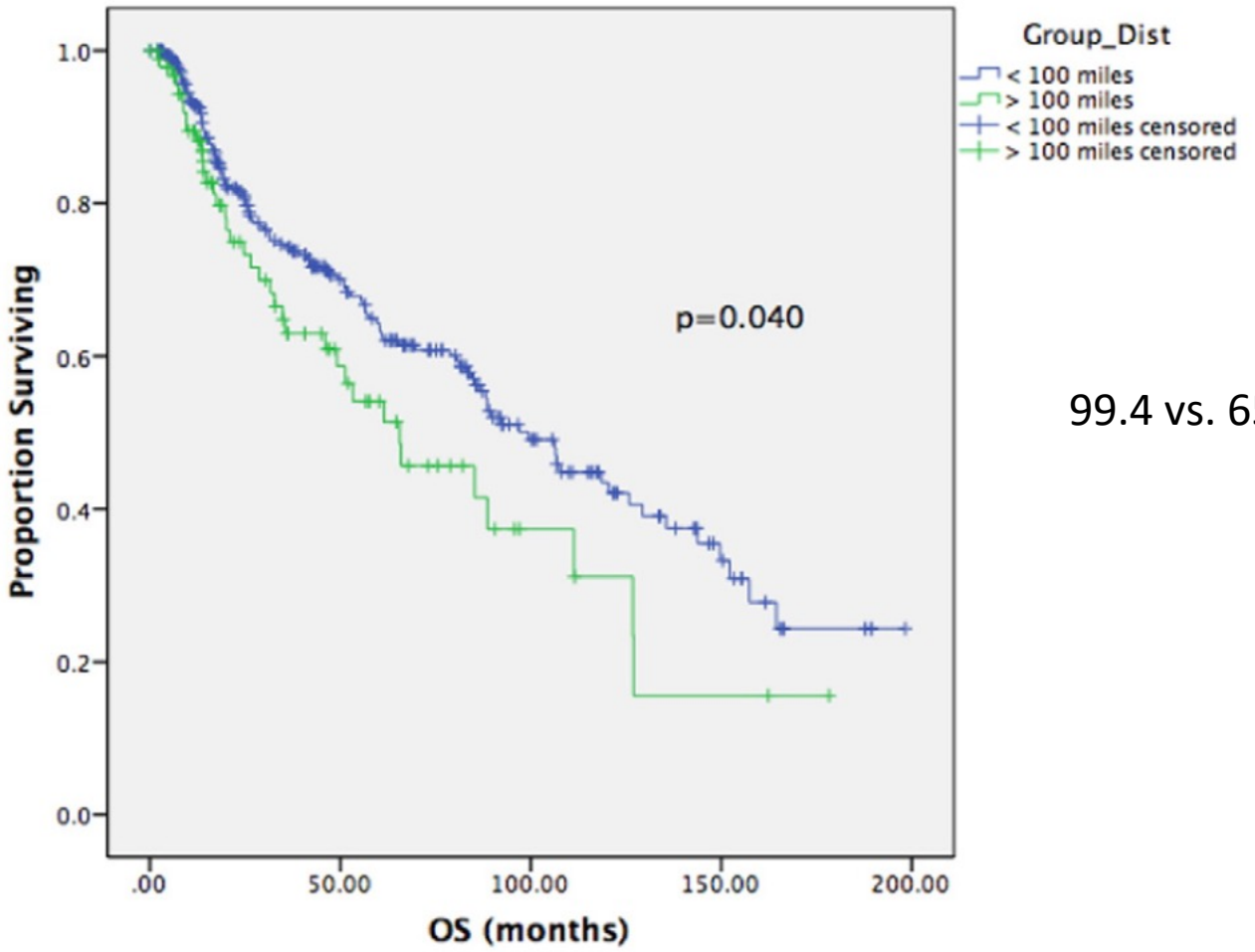


99.4 vs. 65.5 mos

 Barrington DA et al. *Gynecol Oncol* 2016

Advanced Stage Cervical Cancer - Race, Geography and Socioeconomic Factors

- Retrospective cohort from 2005-2015
- Variables
  - Race/Ethnicity
  - Geography – Rural, Urban, Black Belt
  - Distance to ACOG provider
  - Insurance

TABLE 3. Odds of Being Diagnosed With AS Cervical Cancer

	Crude OR	95% CI
Age > 65 y vs. ≤50 y	1.95[b]	1.34–2.84
Black vs. white	1.46[c]	1.09–1.94
Rural vs. urban	1.19	0.91–1.56
Shorter distance to provider	0.99	0.98–1.01
Uninsured[a]	1.40	0.93–2.10
Public insurance[a]	1.80[b]	1.35–2.4
Higher income	0.93	0.85–1.03

 Powell TC et al. *J Low Geni Tract Dis* 2018

FDA grants accelerated approval to tisotumab vedotin-tftv for recurrent or metastatic cervical cancer

Efficacy and safety of tisotumab vedotin in previously treated recurrent or metastatic cervical cancer (innovaTV 204/ GOG-3023/ENGOT-cx6): a multicentre, open-label, single-arm, phase 2 study

*Robert L Coleman, Domenica Lorusso, Christine Gennigens, Antonio González-Martín, Leslie Randall, David Cibula, Bente Lund, Linn Woelber, Sandro Pignata, Frederic Forget, Andrés Redondo, Signe Diness Vindeløv, Menghui Chen, Jeffrey R Harris, Margaret Smith, Leonardo Viana Nicacio, Melinda S L Teng, Annouschka Laenen, Reshma Rangwala, Luis Manso, Mansoor Mirza, Bradley J Monk, Ignace Vergote, on behalf of the innovaTV 204/GOG-3023/ENGOT-cx6 Collaborators**

Coleman RL et al. *Lancet Oncol* 2021

FDA approves pembrolizumab combination for the first-line treatment of cervical cancer

ORIGINAL ARTICLE

Pembrolizumab for Persistent, Recurrent, or Metastatic Cervical Cancer

N. Colombo, C. Dubot, D. Lorusso, M.V. Caceres, K. Hasegawa, R. Shapira-Frommer, K.S. Tewari, P. Salman, E. Hoyos Usta, E. Yañez, M. Gümüş, M. Olivera Hurtado de Mendoza, V. Samouëlian, V. Castonguay, A. Arkhipov, S. Toker, K. Li, S.M. Keefe, and B.J. Monk, for the KEYNOTE-826 Investigators*

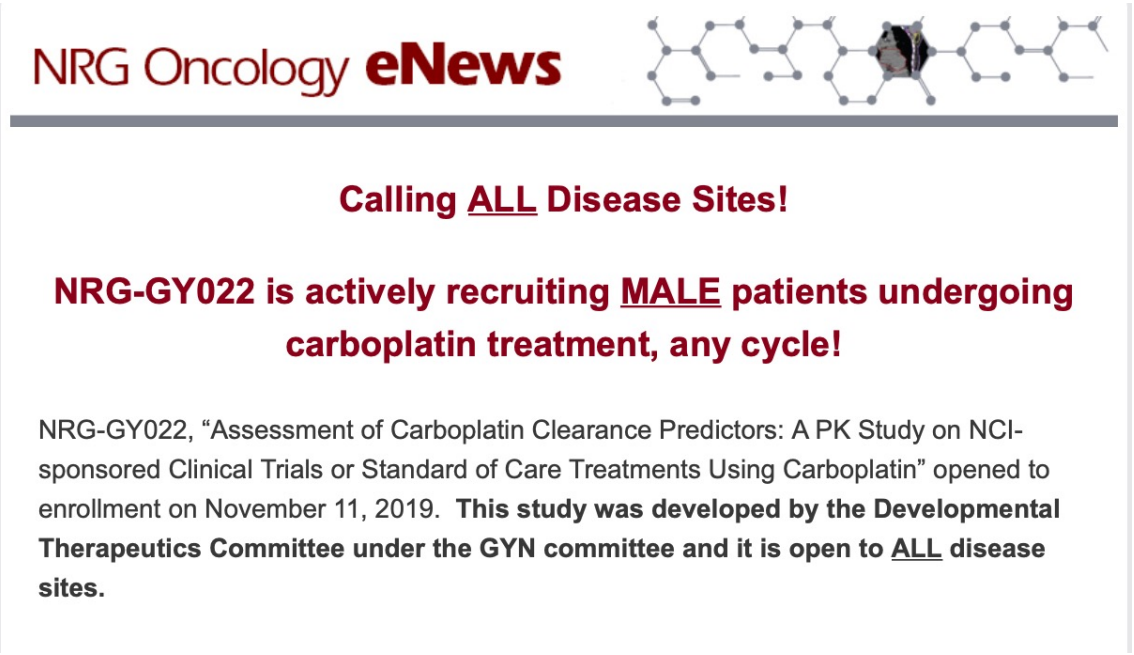
 Colombo N et al. *NEJM* 2021

Conclusions

- NCI sponsored research has had a substantial impact on women with cervical cancer
- Novel approaches may be needed in different geographical regions
- More recent paradigm shifting trials have been performed outside of the NCI
- While therapeutic advances remain important, novel approaches to improve primary vaccination and screening should not be forgotten

Improving cervical cancer clinical trials

- Need representative populations enrolled
  - — Re-evaluate minimum of different racial & ethnic groups?
- Pursue additional research support for enrollment of underrepresented minorities
  - — Bonus credit similar to LAPS versus non–LAPS sites
- “Real world” designs?



NRG Oncology **eNews**

Calling ALL Disease Sites!

NRG-GY022 is actively recruiting MALE patients undergoing carboplatin treatment, any cycle!

NRG-GY022, “Assessment of Carboplatin Clearance Predictors: A PK Study on NCI-sponsored Clinical Trials or Standard of Care Treatments Using Carboplatin” opened to enrollment on November 11, 2019. **This study was developed by the Developmental Therapeutics Committee under the GYN committee and it is open to ALL disease sites.**

Thank you!

O'NEAL COMPREHENSIVE CANCER CENTER
UAB THE UNIVERSITY OF ALABAMA AT BIRMINGHAM

NCI Comprehensive Cancer Center
A Cancer Center Designated by the National Cancer Institute