


Improving Cancer Care for All

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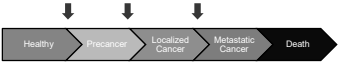


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Outline

- Moonshot
- Improving
 - Prevention
 - Cancer Detection
 - Cancer Treatment
 - Clinical Trials / Implementation



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THE PRESIDENT AND FIRST LADY'S

CANCER MOONSHOT

ENDING CANCER AS WE KNOW IT

Goals of the reignited Cancer Moonshot




- Reduce U.S. cancer death rate by 50% in the next 25 years (by 2047)
- Improve the lives of people and their families living with and surviving cancer

www.whitehouse.gov/cancermoonshot




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Cancer Moonshot: Examples of Progress

In the Cancer Moonshot's first four years (2017-2021):

-  **>2,000** publications
-  **49** clinical trials
-  **>30** patent filings


New Programs

-  **DCCPS Telehealth Research Centers of Excellence (TRACE)**
-  **Cancer Moonshot Scholars**
-  **DCP Multi-Cancer Detection (Vanguard Study)**

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Opportunities to Achieve the Cancer Moonshot "50 by 25" Cancer Mortality Reduction Goal



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Opportunities for Achieving the Cancer Moonshot Goal of a 50% Reduction in Cancer Mortality by 2047

Meredith S. Shiels, Stanley Lipkowitz, Nicole G. Campos, Mark Schiffman, John T. Schiller, Neal D. Freedman, Amy Berrington de González

TO ACHIEVE THE
CANCER MOONSHOT GOAL

**CANCER DEATH RATES
MUST DECLINE FASTER**

| | | |
|--|---|---|
| <small>CURRENT RATE OF DECLINE</small> | ➔ | <small>NEEDED RATE OF DECLINE</small> |
| 2.3% | | 2.7% |
| <small>PER YEAR</small> | | <small>PER YEAR</small> |

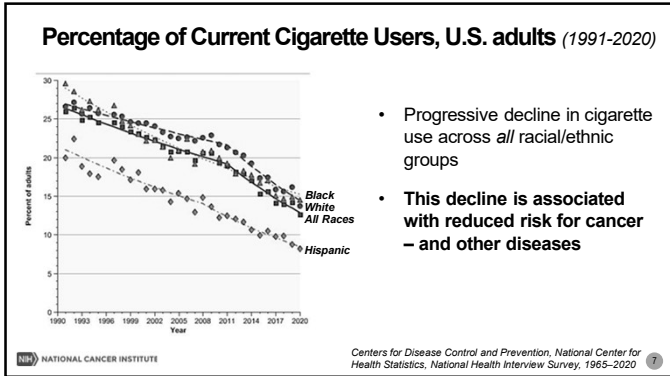
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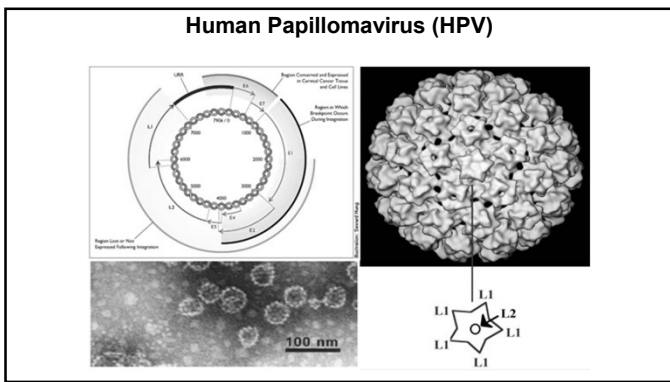


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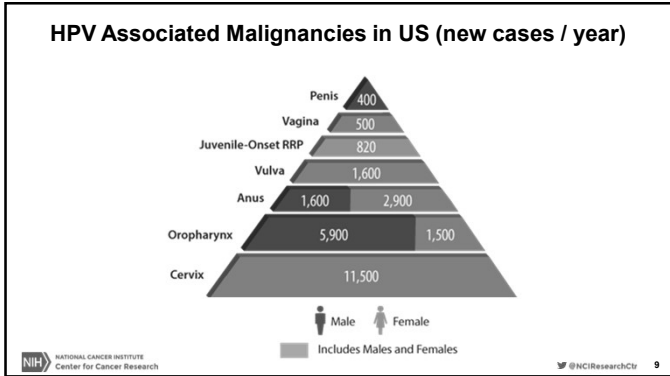
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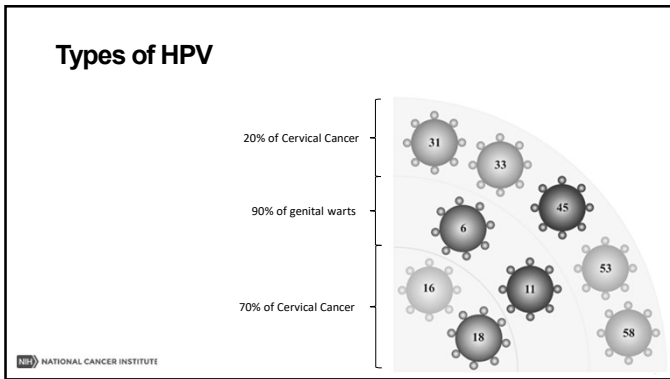
Cervical Carcinogenesis

Normal cervix $\xrightarrow[\text{CLEARANCE}]{\text{INFECTION}}$ HPV-infected cervix $\xrightarrow[\text{REGRESSION?}]{\text{PROGRESSION}}$ Precancer $\xrightarrow{\text{INVASION}}$ Cancer

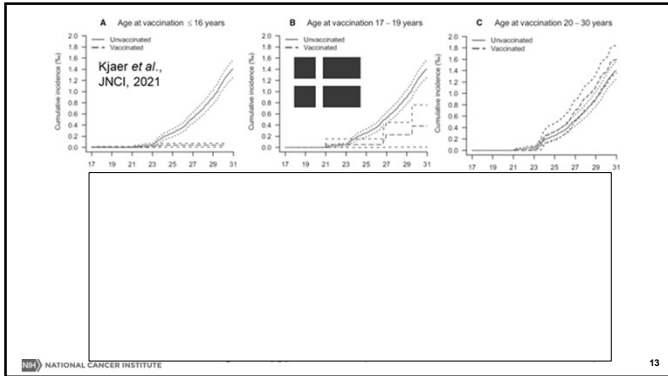
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Lowy and Schiller "took a bold but calculated approach toward a major public health problem which solution required them to vault formidable hurdles."
--Lasker Foundation

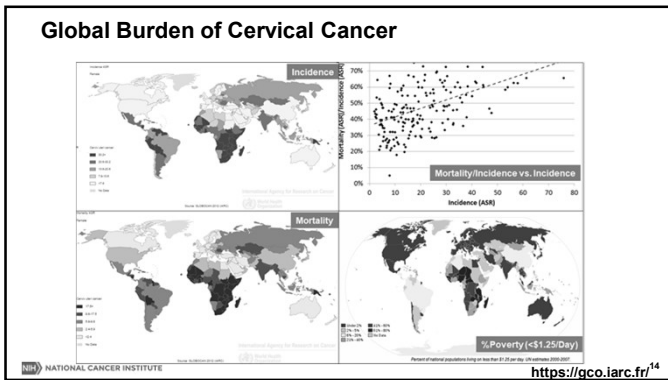
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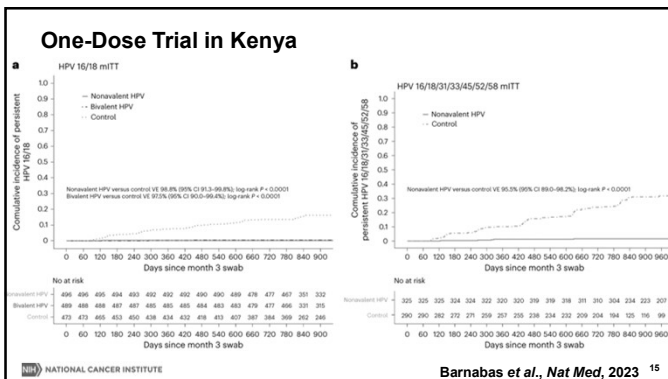
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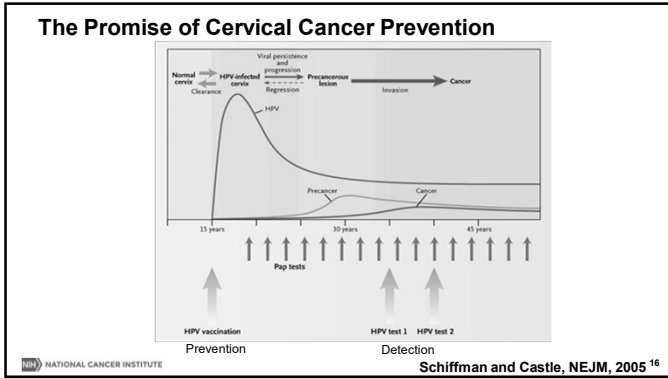
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World Health Organization Strategy to Eliminate Cervical Cancer as a Public Health Problem

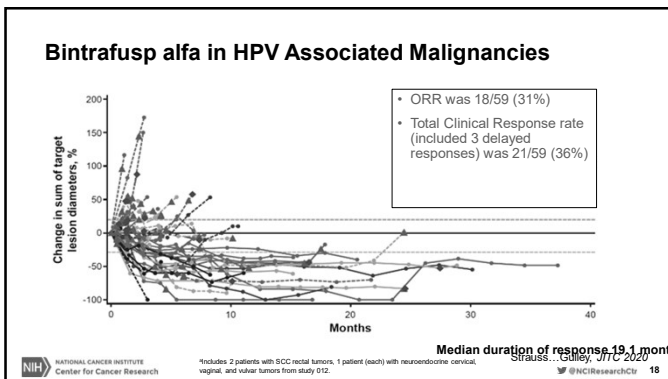
- 90% of girls fully vaccinated with the HPV vaccine by the age of 15 years;
- 70% of women screened using a high-performance test* by the age of 35 years and again by the age of 45 years; and
- 90% of women identified with cervical disease receive treatment (90% of women with pre-cancer treated and 90% of women with invasive cancer managed).

<https://www.who.int/initiatives/cervical-cancer-elimination-initiative>

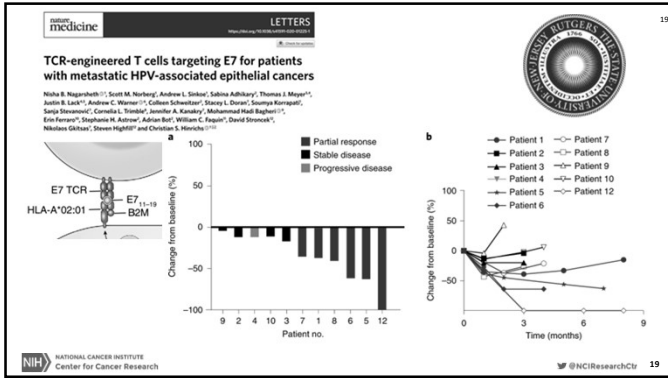
*WHO recommends using HPV DNA detection as the primary screening test rather than VIA or cytology in screening and treatment approaches among both the general population of women and women living with HIV (<https://www.who.int/publications/i/item/9789240030824>)

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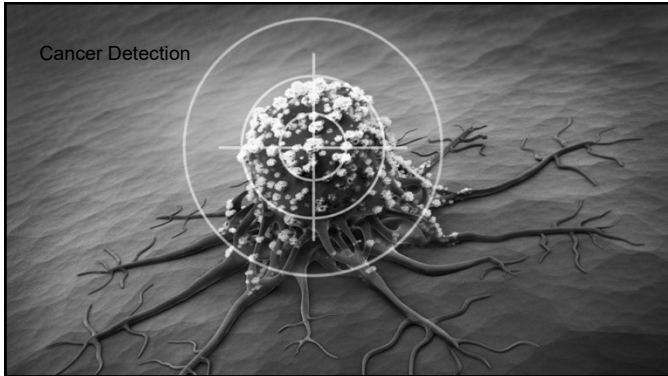


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Prevention

- Prevention studies are difficult to do, require a lot of patients (and patience).
- Then you must implement findings
 - HPV vaccine early (by 15 y/o) to have maximal impact

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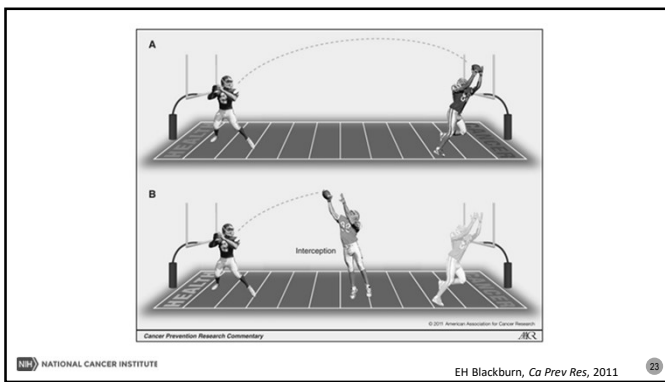
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Systematic Review of Smoking Cessation Interventions

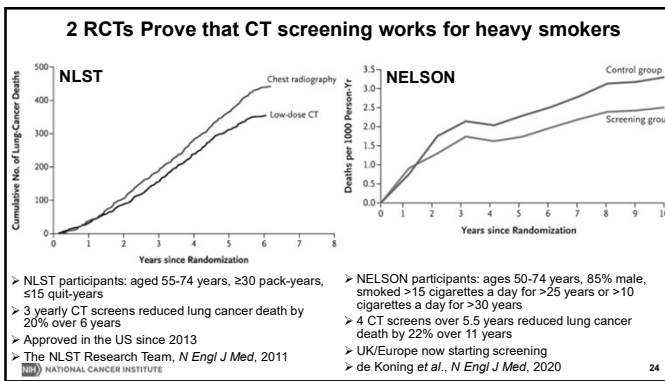
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|---|---|--|--|--|
| <p>Combined pharmacotherapy and behavioral</p> <p>1 review (1 RCT, n = 25,373)</p> | <p>Combined pharmacotherapy and behavioral interventions increased smoking quit rates by 60% to 80% compared with no or minimal treatment (RR, 1.63 [95% CI, 1.48-1.80]) at mid-follow-up.</p> | <p>Reasonably consistent, reasonably precise</p> | <p>May be risk of bias due to lack of blinding of participants</p> | <p>High evidence of benefit*</p> |
| <p>Pharmacotherapy</p> <p>5 reviews (16 RCTs, n = 159,000)</p> | <p>NRT, bupropion, and varenicline significantly increased the chances of quitting smoking compared with placebo or no medication.</p> <p>Reviews suggested that NRT might increase smoking abstinence at 6 mo or longer by 49% to 61% (RR, 1.55 [95% CI, 1.41-1.71]), bupropion by 49% to 76% (RR, 1.62 [95% CI, 1.49-1.76]), and varenicline by 100% to 147% (RR, 2.24 [95% CI, 2.06-2.43]).</p> <p>Absolute quit differences averaged 6.4% for NRT, 8.2% for bupropion, and 14.4% for varenicline.</p> <p>Using a combination of NRT products increased quitting more than the use of a single NRT product (RR, 1.25 [95% CI, 1.13-1.38]).</p> <p>Direct comparisons between drugs suggested that varenicline may be superior to NRT and bupropion in achieving smoking abstinence at 6 mo.</p> | <p>Reasonably consistent, reasonably precise</p> | <p>Possibility of publication bias but unlikely that the presence of additional studies will lower relative risks would alter the findings, given large number of studies and consistency in findings for each type of drug.</p> | <p>High evidence of benefit*</p> |
| <p>Behavioral</p> <p>20 reviews (830 RCTs, n = 500,000)</p> | <p>Clinical advice and counseling, individual counseling, group-based interventions, telephone counseling, mobile phone-based interventions, laboratory and interactive Internet-based interventions, and incentives showed significant increased smoking cessation at 6 mo or more relative to controls (1.15-1.85); for example, 86% (95% CI, 1.58-1.96) for physician advice to minimal controls or usual care.</p> <p>Providing more intense, adjunctive behavioral support to smokers receiving pharmacotherapy may increase cessation by 8% to 27% (RR, 1.13 [95% CI, 1.09-1.22]).</p> <p>Evidence on the use of motivational interviewing, decision aids, print-based, extended self-help materials, real-time video counseling, biomedical risk assessment, exercise, complementary and alternative therapies, and system-level interventions was limited and not attributable to the effects on cessation.</p> | <p>Reasonably consistent, Reasonably precise</p> | <p>Individual trials may be represented in more than 1 review and/or meta-analysis.</p> <p>Indication of possible publication bias for evidence related to motivational interviewing and acupuncture.</p> <p>Fixed-effects models were used in nearly all meta-analyses.</p> | <p>Moderate to high evidence of benefit*</p> |

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USPSTF updated lung cancer screening recommendations
(March 2021)

Annual screening for lung cancer with low-dose CT in adults aged **50 to 80 years** who have a **20 pack-year smoking history** and currently smoke or have quit within the past 15 years

Previously:
55 to 80 years who have a **30 pack-year smoking history**

- * Increase in population **eligible** for screening: From **14%** (of 1960 birth cohort) to **23%**
- * Improves equity: a higher proportion of women and under-represented minorities

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Recent Estimates of Lung Cancer Screening USPSTF 2013 Guidelines

By 2019 and 2020, according to ACR LCSR, up-to-date lung cancer screening rates progressed to 6.5%-6.6% or about 560 thousand screened of 8.5 million eligible.

In the BRFSS, estimates are higher at 16.3% overall in 2017-2020; estimates ranged from 7% in Utah to 21% in Vermont among 20 states that measured LCS in 2019.

American Cancer Society

Chest, Volume 151, Issue 2, February 2022, Pages 586-589, https://doi.org/10.1016/j.chest.2021.07.030

BRFSS LCSR

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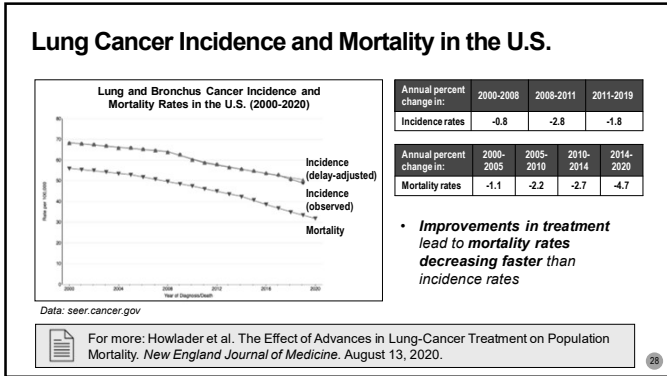
Joint Lung Cancer Screening & Cessation Interventions Under New USPSTF Recommendations

Joint screening and cessation interventions would result in considerable life-years gained and deaths averted

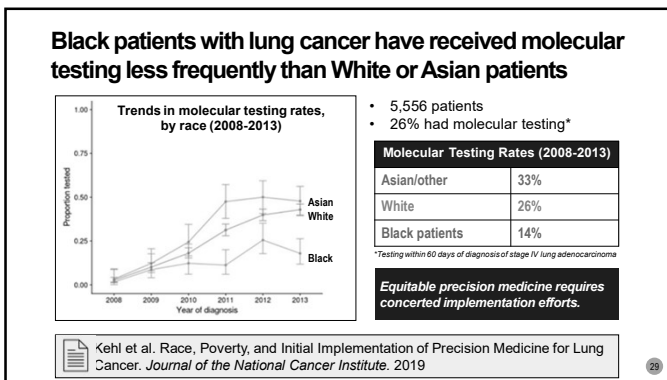
Meza R, Cao P, Jeon J, et al. Impact of Joint Lung Cancer Screening and Cessation Interventions Under the New Recommendations of the U.S. Preventive Services Task Force. J Thorac Oncol. 2021;S1556-0864(21)03208-1.

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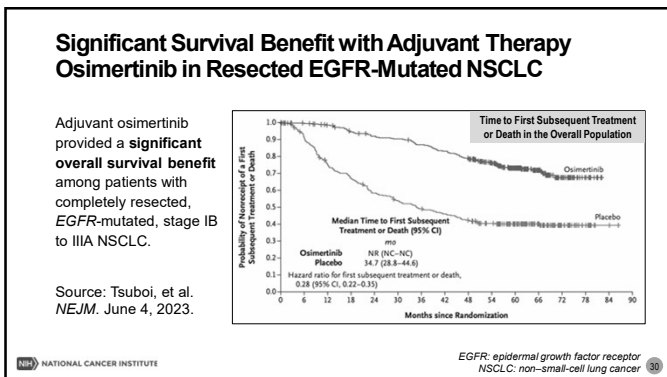
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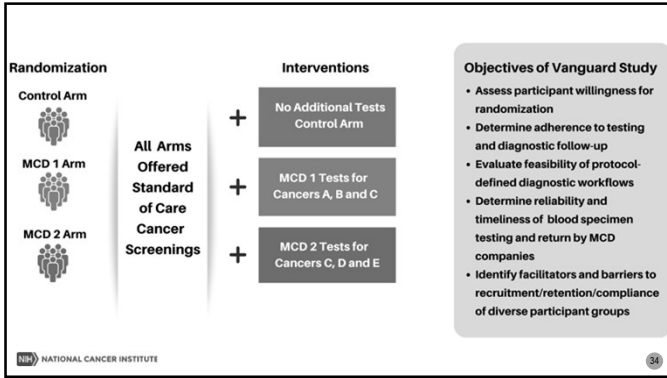
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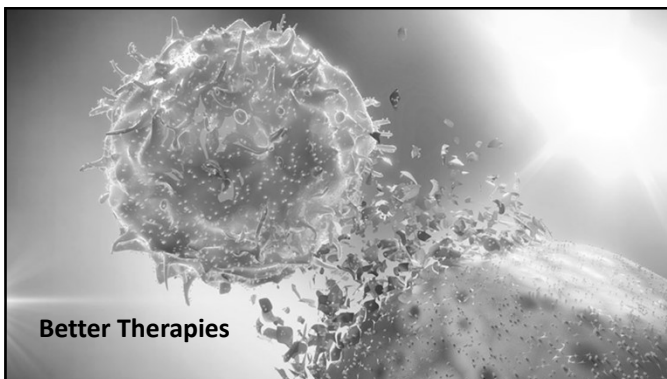
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Detection

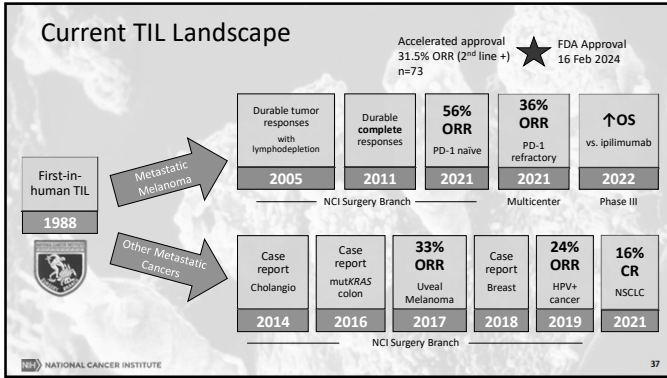
- Earlier detection can lead to interception of cancer when it is more likely to be curable.
- Implementation of currently established guidelines for screening could accelerate decline of cancer related mortality
- MCD offer the potential to revolutionize cancer screening, but there is insufficient data to understand how best to use them.
- NCI's new Cancer Screening Research Network (CSRN), part of the Cancer Moonshot, is positioned to carry out studies evaluating new screening modalities throughout the US (Vanguard Study).

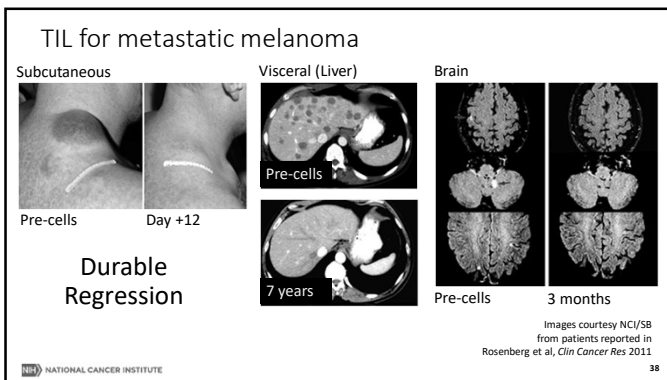
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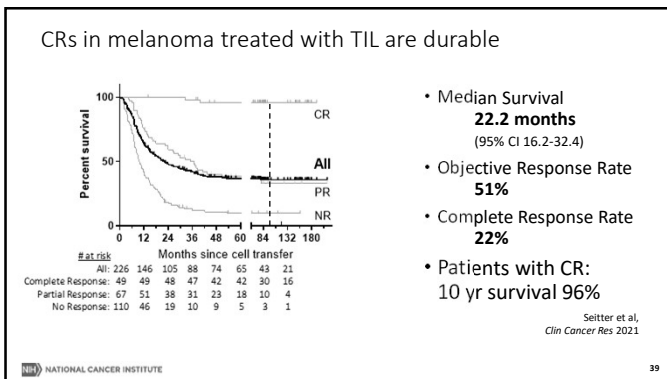
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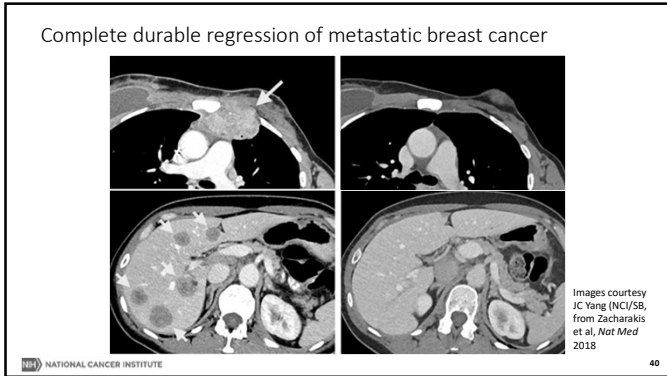


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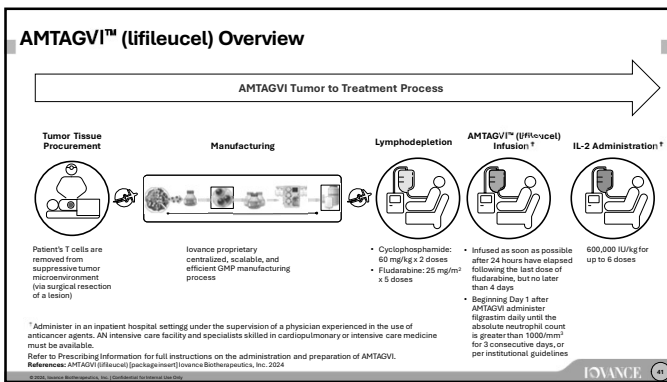








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Patient Selection Considerations

An intraoperative strategy that **minimizes perioperative morbidity is crucial**, as the tumor resection for TIL cell therapy is **not therapeutic**¹

C-144-01: Inclusion Criteria¹

- Age ≥ 18
- Unresectable or metastatic melanoma (stage IIC or stage IV) per American Joint Committee on Cancer
- At least one prior line of systemic therapy with a PD-1 block antibody containing therapy, and if BRAF mutation positive, BRAF +/- MEK inhibitor
- ECOG performance status of 0 or 1
- Adequate organ function and hematologic parameters
- ≥1 resectable lesion(s) providing resected tumor tissue ≥1.5 cm in diameter to generate TIL cell therapy and ≥1 remaining target lesion, as defined by RECIST v1.1
- No brain mets, or definitively treated brain mets
- Estimated life expectancy of ≥ 3 months

C-144-01: Exclusion Criteria¹

- Organ allograft or prior cell transfer therapy
- Uveal/Ocular melanoma
- Symptomatic and/or untreated brain metastases
- Chronic system steroid therapy
- Active systemic infections
- Administration of live or attenuated vaccine within 28 days of lymphodepletion
- Chronic heart (ejection fraction < 45%) or lung abnormality (forced expiratory volume ≤ 60%)

ECOG PS=Eastern Cooperative Oncology Group performance status, TIL=tumor-infiltrating lymphocytes.
References: 1. Chenail, et al. J Immunother Cancer 2022; 10(7): 1-14.

IOVANCE

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Surgical Site Selection Considerations: Mullinax JE, et al. Review Article ¹

Anatomic resection sites which minimize morbidity and can be performed in the outpatient setting should be considered¹

Commonly Resected Sites¹

- Skin
- Soft Tissue
- Superficial Lymph Nodes

Additional Sites¹

- Smaller Nodules Within Visceral Organs (e.g., Liver, Lung)
- Peripheral Lesions

Less Optimal Sites¹

- Secondary Lymphoid Organs
- GI Tract

In a post-hoc exploratory analysis of the C-144-01 trial, lifileucel could be manufactured regardless of anatomic site of tumor resection and anatomic site did not correlate with infused dose.²

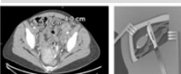
AC2:Resective of therapy (Organ of Assessment): TL: tumor site (e.g., lymph node)
 Reference: 1. Mullinax JE, Egger HE, McCarter M, et al. Cancer (2022)25:295-303. 2. Egger HE, Lifileucel TL Cell Therapy in Patients With Advanced Melanoma After Progression on Immune Checkpoint Inhibitors (C3) and Targeted Therapy: Tumor Resection Data From the C-144-01 Study. 2023.
 © 2023, Iovance BioPharmaceuticals, Inc. (Iovance BioPharmaceuticals)

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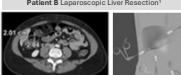
Image-Guided Approach for Lesion Selection May Help Mitigate Surgical Complications

- **Image-guided approaches & minimally invasive procedures¹**
 - May mitigate the complications and recovery associated with open resection
- **Image-guided techniques may be considered for:**
 - Complex anatomic locations (eg, spine and pelvis)¹
 - Urologic tumors¹
 - Reducing morbidity and mortality²
- **MRI-guided percutaneous biopsy¹**


Patient A Lymph Node Open Excision¹



Patient B Laparoscopic Liver Resection¹



Patient C VATS Resection of Lung Nodule¹



CT:contrast media; biopsy: HB;imaging: MRI;imaging:TL;tumor site (e.g., lymph node); VATS:video-assisted thoracoscopic surgery
 Reference: 1. Mullinax JE, Egger HE, McCarter M, et al. Cancer (2022)25:295-303. 2. Gostrom B, Agreus P, Berger A, et al. J Immunother Cancer (2023) e01593.
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Best Practices to Avoid Contamination of the Tumor Tissue

Sites that have been previously irradiated, those with ulcerated tumors, or those with high risk of bacterial growth (e.g., bowel lesions), could lead to contamination of tumor cultures and should be avoided when possible¹

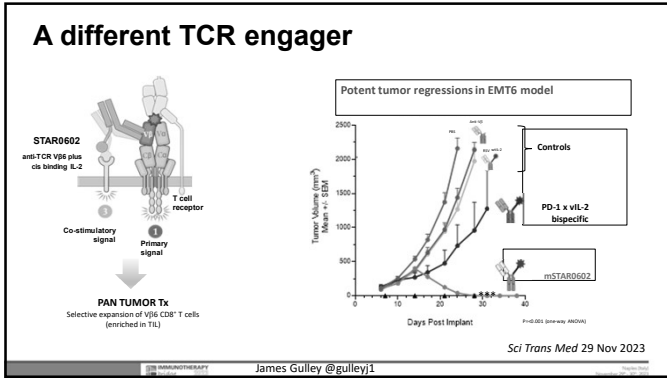
Risk of tumor tissue contamination can be mitigated with OR procedures akin to those for organ transplantation²

- OR equipment and any instruments that may contact tumor tissue must be **sterile¹**
- **Prosection** should be accomplished by the **operating surgeon¹**
- Tumor tissue should **leave the OR** only after **prosection has been completed^{1,2}**
- **Tumor tissue** should be sealed in a **sterile media transfer container^{1,2}**
- Tumor material used by pathology should be **handled separately** and not used for TIL generation

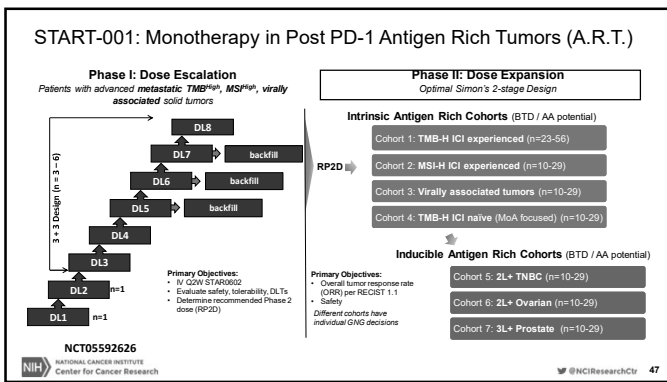
- Tumor types that co-locate in **higher-bioburden areas** have the possibility for contamination²

OR:operating room; TL:tumor site (e.g., lymph node)
 Reference: 1. Mullinax JE, Egger HE, McCarter M, et al. Cancer (2022)25:295-303. 2. Egger HE, Lifileucel TL Cell Therapy in Patients With Advanced Melanoma After Progression on Immune Checkpoint Inhibitors (C3) and Targeted Therapy: Tumor Resection Data From the C-144-01 Study. 2023.
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AI→Clinical Trial Innovation

- Consents
- Case Report Form (eCRF)
- Immune-Related Adverse Events (irAE)

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Participant Consent Forms

Using Generative AI to Create First Drafts & Simplify Existing Content

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Participant Consent Forms

- Use Standardized Templates
- Customizable based on study type and population
- Challenges
 - Time consuming to write
 - Difficult to write at the appropriate reading level
- Aims
 - Reduce overall length by 20%
 - Overall Flesch-Kincaid reading level: 6th grade
 - Flesch Reading Ease ≥ 70 (easy to very easy to read)



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Consents

- Divide template into sections
- Simplify the modifiable sections
- Reconstruct the consent

Example:

| | | |
|---|------------------------------|--|
| Overall Reading Level 10th Grade | 11th Grade | Not Modifiable: <ul style="list-style-type: none"> •Site-specific required •Legally required •Study title •Contact information |
| | 9th Grade | Modifiable (Study-specific Language) <ul style="list-style-type: none"> •Study Description and key information •Risks and discomforts •Benefits •Withdrawal |
| | 9th Grade | Partially Modifiable <ul style="list-style-type: none"> •Combination sections with required text intermingled with study-specific language |

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Use Case Example: Key Information About a Study

Original

Lines: 77
Grade level: 11.7
Reading ease: 52.0

Example text:
First, we will perform tests to find out if you fit the study requirements. We will do standard blood tests and scans to test your health and see the status of your disease. You will also be asked to provide documentation to confirm your diagnosis. If documentation or a sample of your tumor is not available, we will perform a biopsy (collect a sample of your tumor) to confirm your diagnosis.

➔

Simplified

Lines: 58 (+25%)
Grade level: 7.2
Reading ease: 73.8

Example text:
"First, we will do tests to see if you can join the study. We will check your blood and do scans to see how your health is and how your cancer is doing. You will need to give us papers to confirm your cancer. If we can't get those papers or a sample of your tumor, we will take a small piece of your tumor to confirm your cancer."
GPT-4


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Using a Large Language Model to Extract Common Data Elements for Case Report Forms

Case data are manually abstracted from clinical notes:

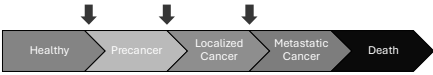
- Time consuming
- Prone to human error

Aim to utilize AI to extract common data elements from clinical text and identify adverse events for reporting, lab data, clinical outcomes data



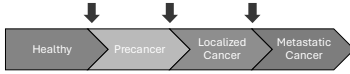
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Conclusions



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Conclusions



- Special Thanks to
 - Phil Castle DCP, NCI
 - Bill Dahut ACS
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 - Tanna Nelson CCR, NCI
 - Kim Rathmell NCI
