ASTRO 2023

# PAY IT FORWARD

PARTNERING WITH OUR PATIENTS

## ASTRO 65TH ANNUAL MEETING

**October 1-4, 2023**

San Diego Convention Center

San Diego

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# Welcome

# HPV Circulating Cell-Free DNA Kinetics in Cervical Cancer Patients Undergoing Definitive Chemoradiation

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10/01/23

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Making Cancer History®

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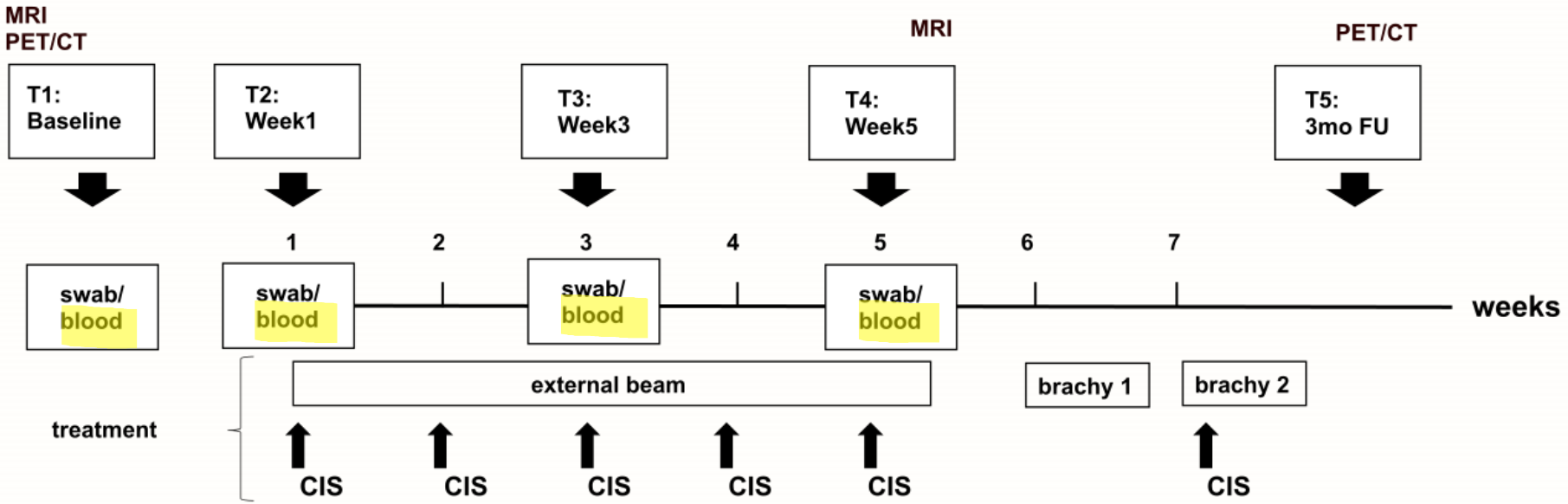
# Disclosure

I have no conflicts of interest to disclose

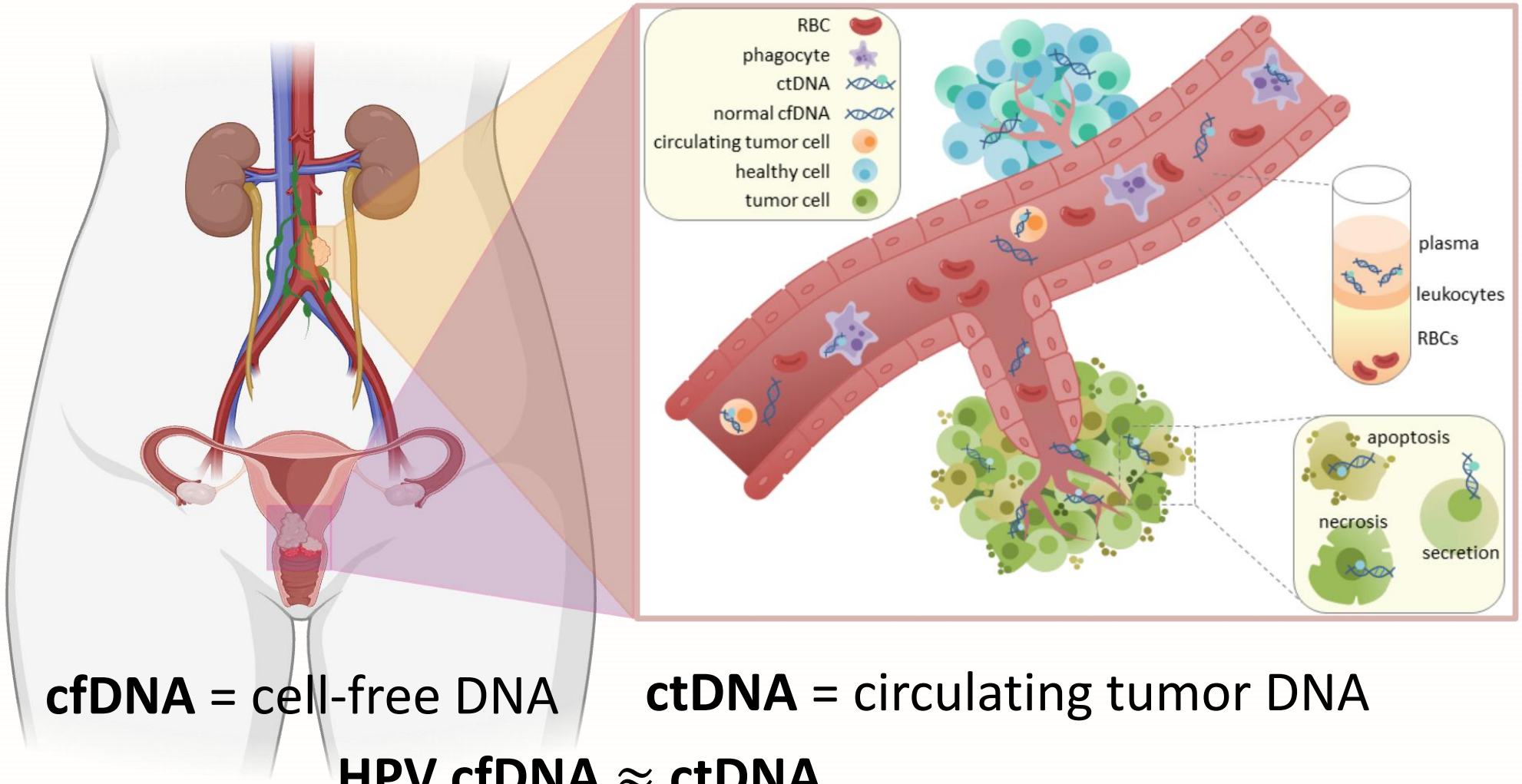
# Background

## MDACC Cervical Cancer Definitive Treatment: Timeframe & Data Collection




- Many different ongoing translational projects
- **Needs**: Refined prognostication, Assessing treatment response, Surveillance
- **Today's focus**: Describing changes in HPV cell-free DNA during/after treatment

# Background




**cfDNA** = cell-free DNA **ctDNA** = circulating tumor DNA

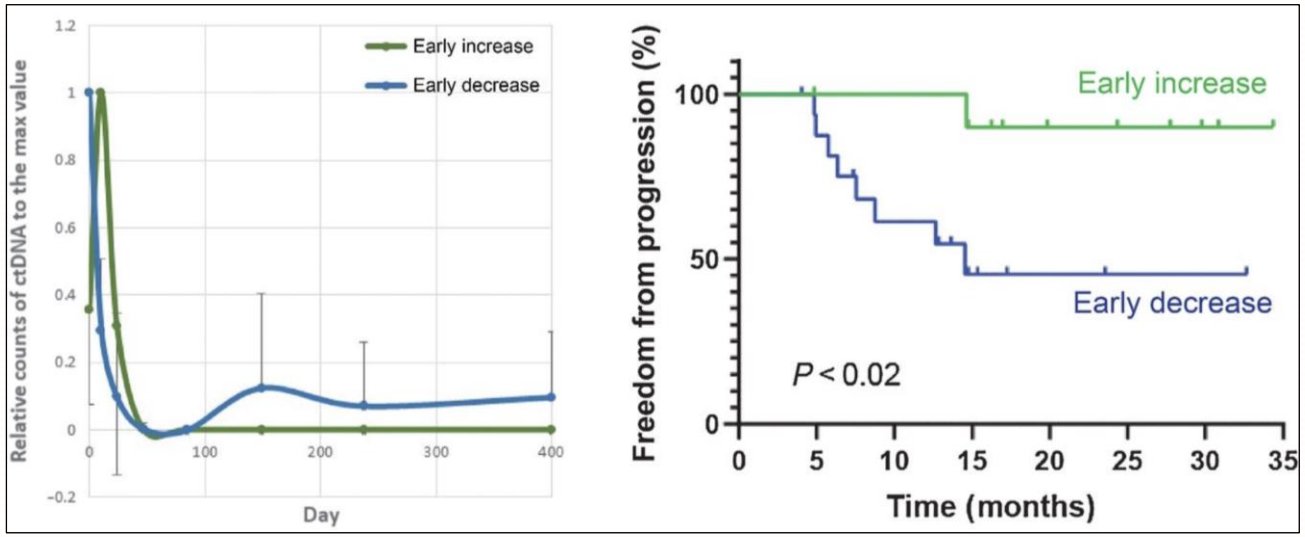
**HPV cfDNA ≈ ctDNA**

Adapted from Racheljunewong (Creative Commons) on BioRender

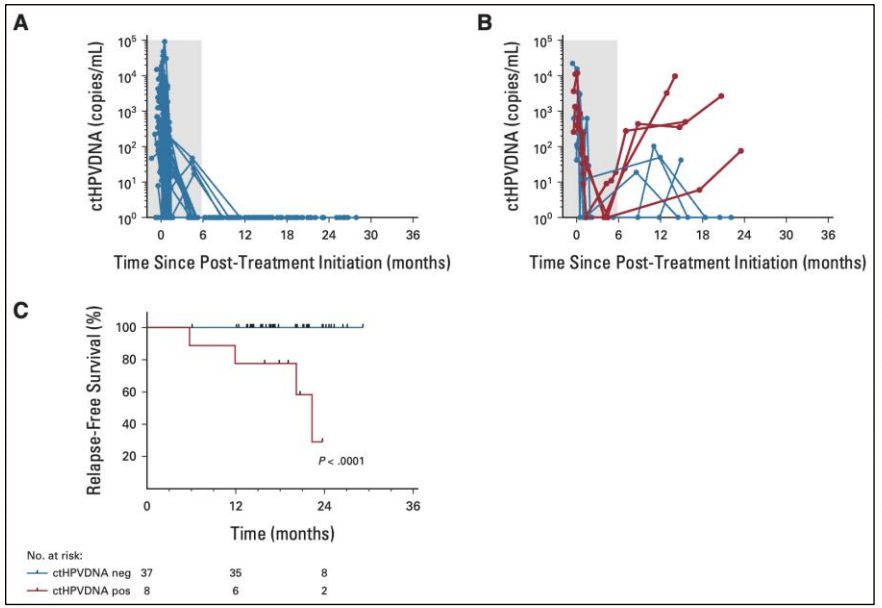
# Background

## HPV+ Oropharyngeal Cancers

### Intra-treatment Monitoring (chemoRT)[1]




### Post-treatment Surveillance[2]

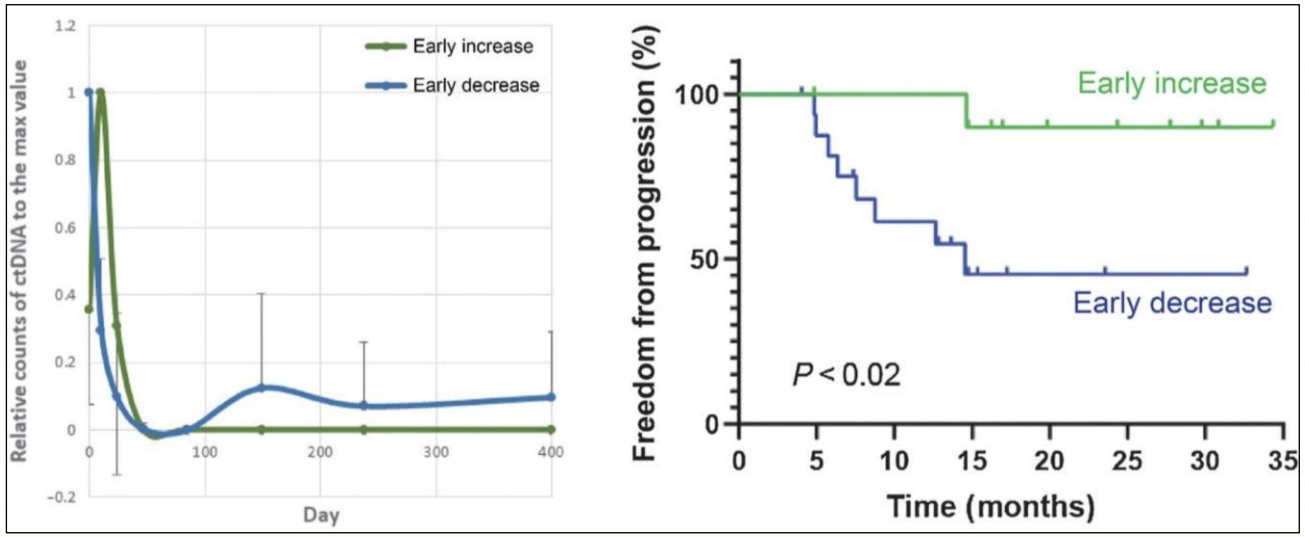



[1]Cao *Clin Cancer Res* 2022
[2]Chera *JCO* 2020

# Background

## HPV+ Oropharyngeal Cancers

### Intra-treatment Monitoring (chemoRT)[1]

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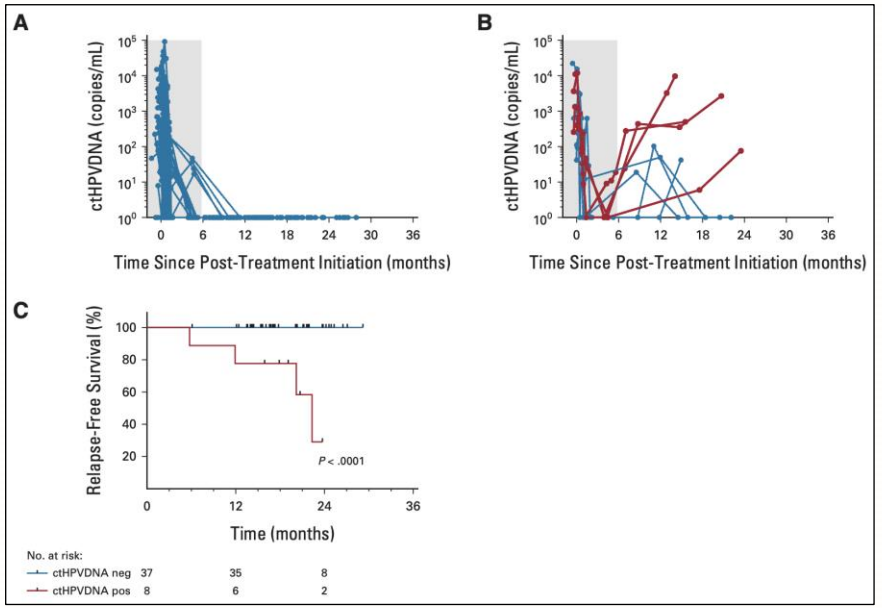
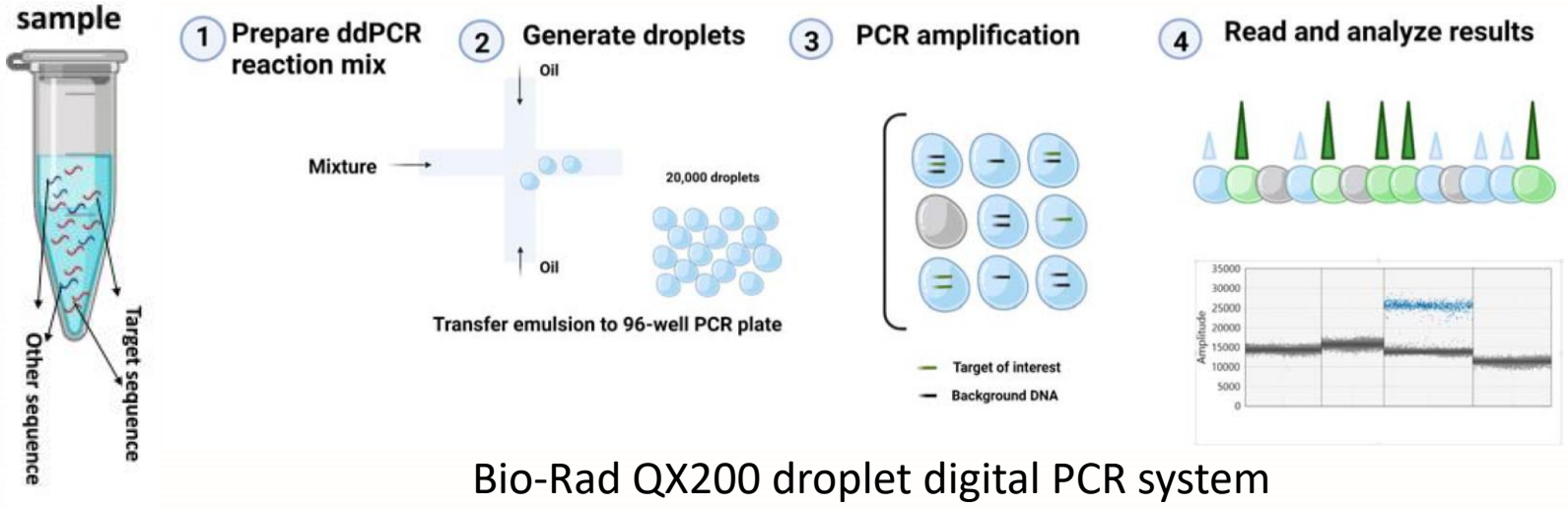



HPV+ cervical cancers?

[1]Cao *Clin Cancer Res* 2022
[2]Chera *JCO* 2020

# ddPCR Assay

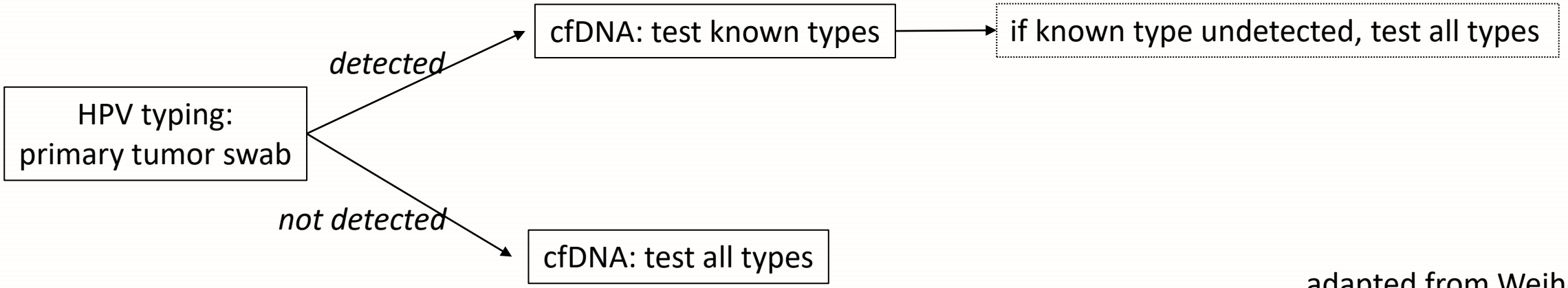



Bio-Rad QX200 droplet digital PCR system

## Gillison Lab

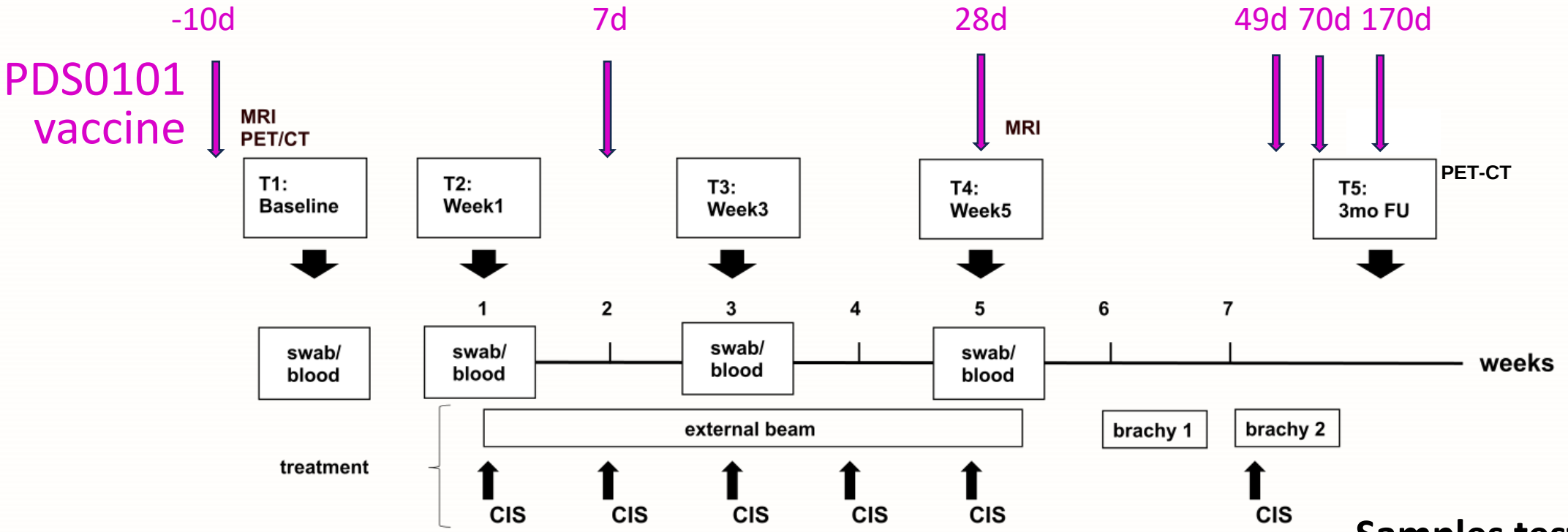
13 HPV types tested:
16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68

Limit of Detection (LoD): 16 copies/mL




adapted from Weihong Xiao
Lambrescu *Int. J. Mol. Sci.* 2022

# Cohorts: SOC vs PDS0101




**Samples tested for cfDNA?**

**SOC**: Standard-of-care — 44 pts

**PDS0101**: Phase IIA IMMUNOCERV trial PDS0101 therapeutic vaccine (HPV-16 E6/E7 antigen), *ongoing* — 17 pts

**61 total**

# Cohort Characteristics

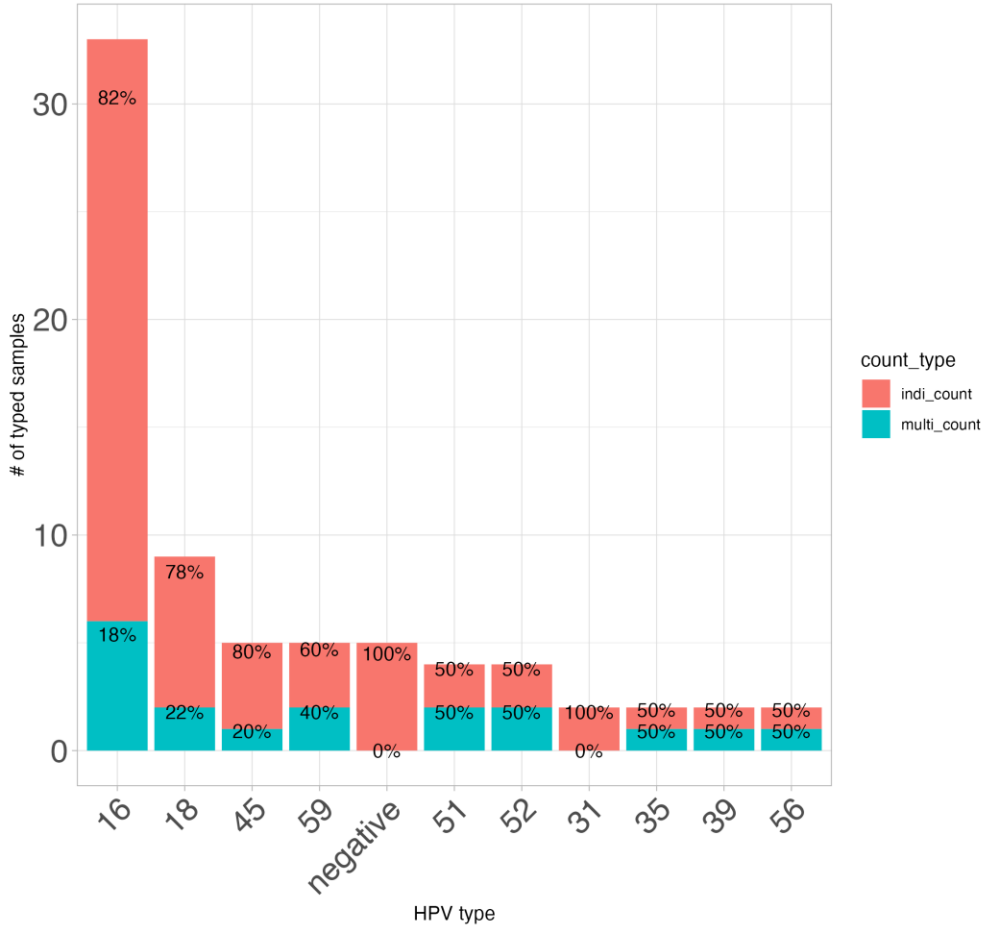
| Characteristic | SOC | PDS0101 | P-value |
|---|---|---|---|
| **Age** (yrs;mean) | 43.9 | 44.1 | 0.96 |
| **BMI** (kg/m$^2$;mean) | 29.6 | 26.7 | 0.04 |
| **Ethnicity**, *n(%)* | | | 0.18 |
| Hispanic/Latino | 13(30%) | 2(12%) | |
| Not Hispanic/Latino | 30(68%) | 14(82%) | |
| Declined to answer | 1(2%) | 1(6%) | |
| **Smoking Status** | | | 0.71 |
| Current | 6(14%) | 2(12%) | |
| Former | 10(23%) | 6(35%) | |
| Never | 26(59%) | 9(53%) | |
| Unknown | 2(4%) | 0(0%) | |

| Characteristic | SOC | PDS0101 | P-value |
|---|---|---|---|
| **FIGO 2018 Stage** | | | 0.80 |
| I | 3(7%) | 1(6%) | |
| II | 8(19%) | 2(12%) | |
| III | 29(69%) | 12(71%) | |
| IV | 2(5%) | 2(12%) | |
| **Nodal Involvement** | | | 0.02 |
| Yes | 31(70%) | 17(100%) | |
| No | 11(25%) | 0(0%) | |
| Unknown | 2(5%) | 0(0%) | |
| **Highest Involved Node** | | | 0.14 |
| Para-Aortic | 9(29%) | 2(12%) | |
| Common Iliac | 8(26%) | 2(12%) | |
| Other Pelvic | 14(45%) | 13(76%) | |

Difference in % nodal involvement (greater in PDS0101)

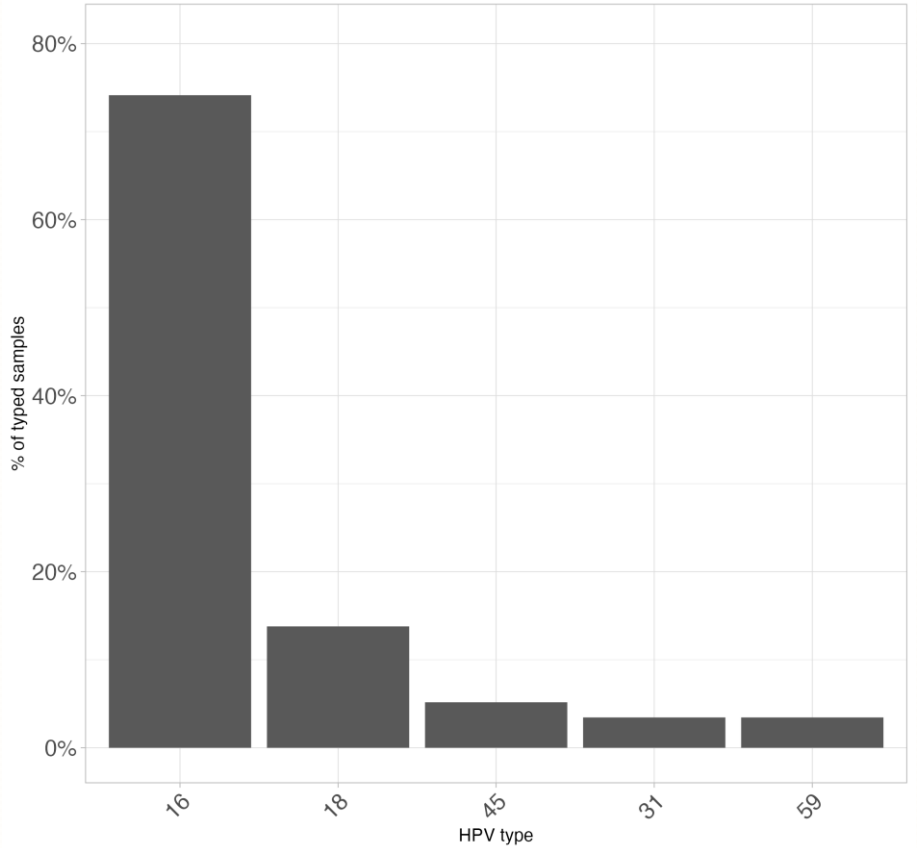
# HPV Types: Tumor & cfDNA

## HPV types detected in tumor



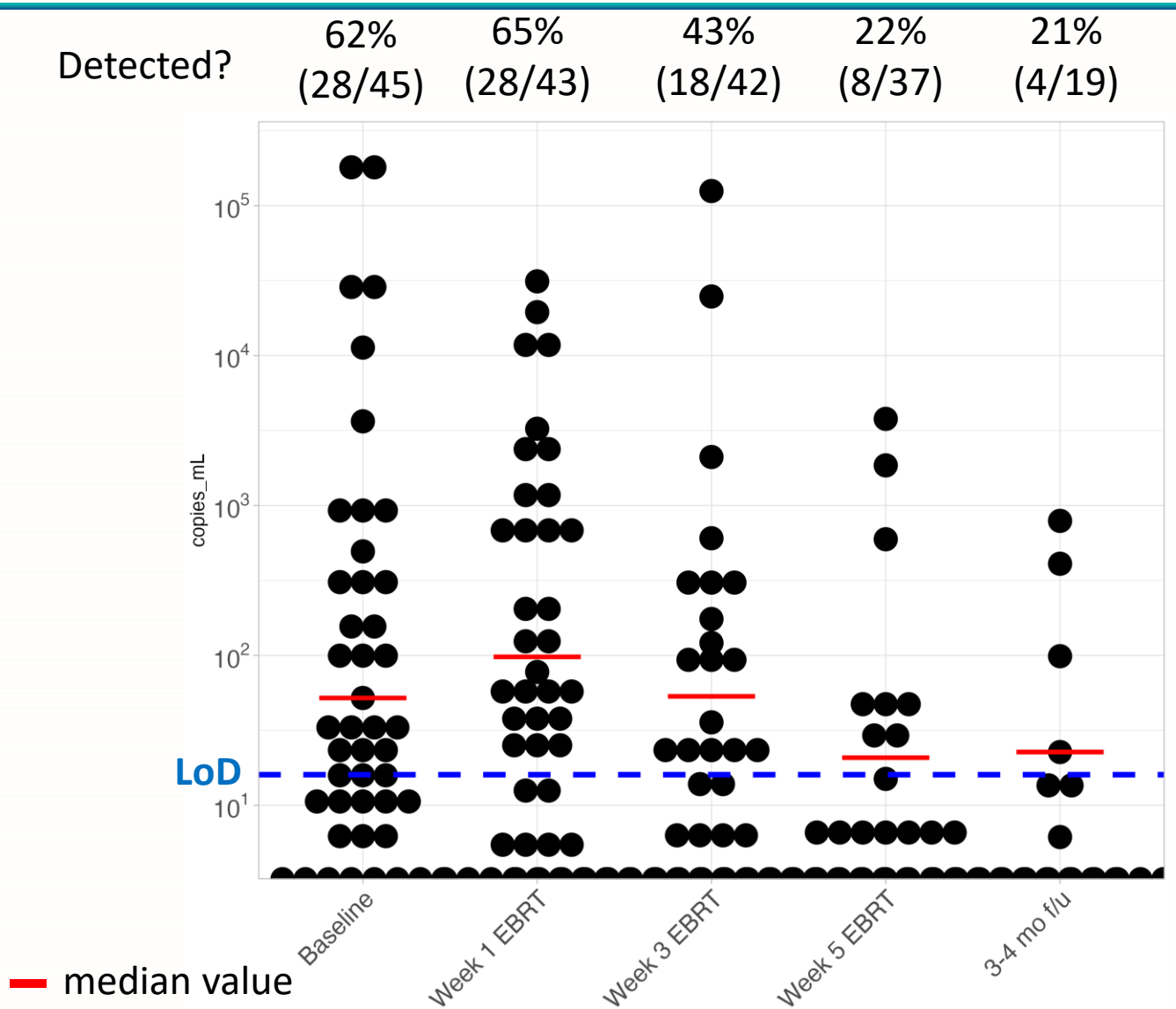

- HPV-16+: 59% (27/46) of pts
- HPV-negative: 11% (5/46) of pts

## HPV types detected in cfDNA




- HPV-16 detected in 70% (43/61) of pts (74% of pts w/ HPV type+)
- No HPV cfDNA detected in 5% (3/61) of pts

# HPV cfDNA Distribution During and After RT




Cohorts Pooled

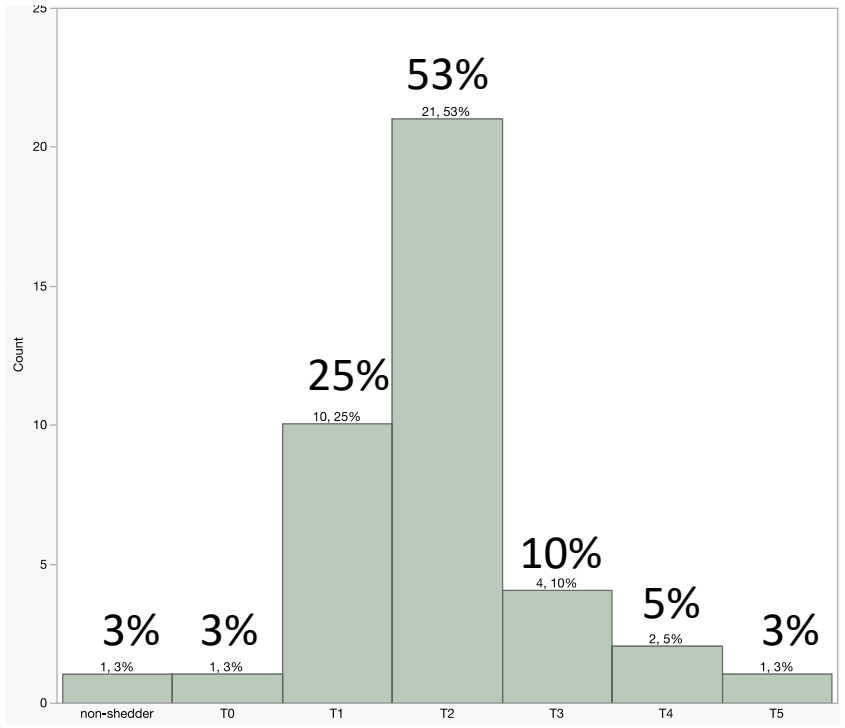
| Timepoint | Median (copies/mL) | Range |
|---|---|---|
| Before EBRT (T1) | 28.15 | 0 - 206,030 |
| Week 1 EBRT (T2) | 48.92 | 0 - 31,255 |
| Week 3 EBRT (T3) | 7.06 | 0 - 125,155 |
| Week 5 EBRT (T4) | 0 | 0 - 3780 |
| 3-4 mo f/u (T5) | 0 | 0 - 789 |

- HPV cfDNA detection changes over time
- Wide range of HPV cfDNA levels

**LoD**: limit of detection **EBRT**: external beam radiotherapy

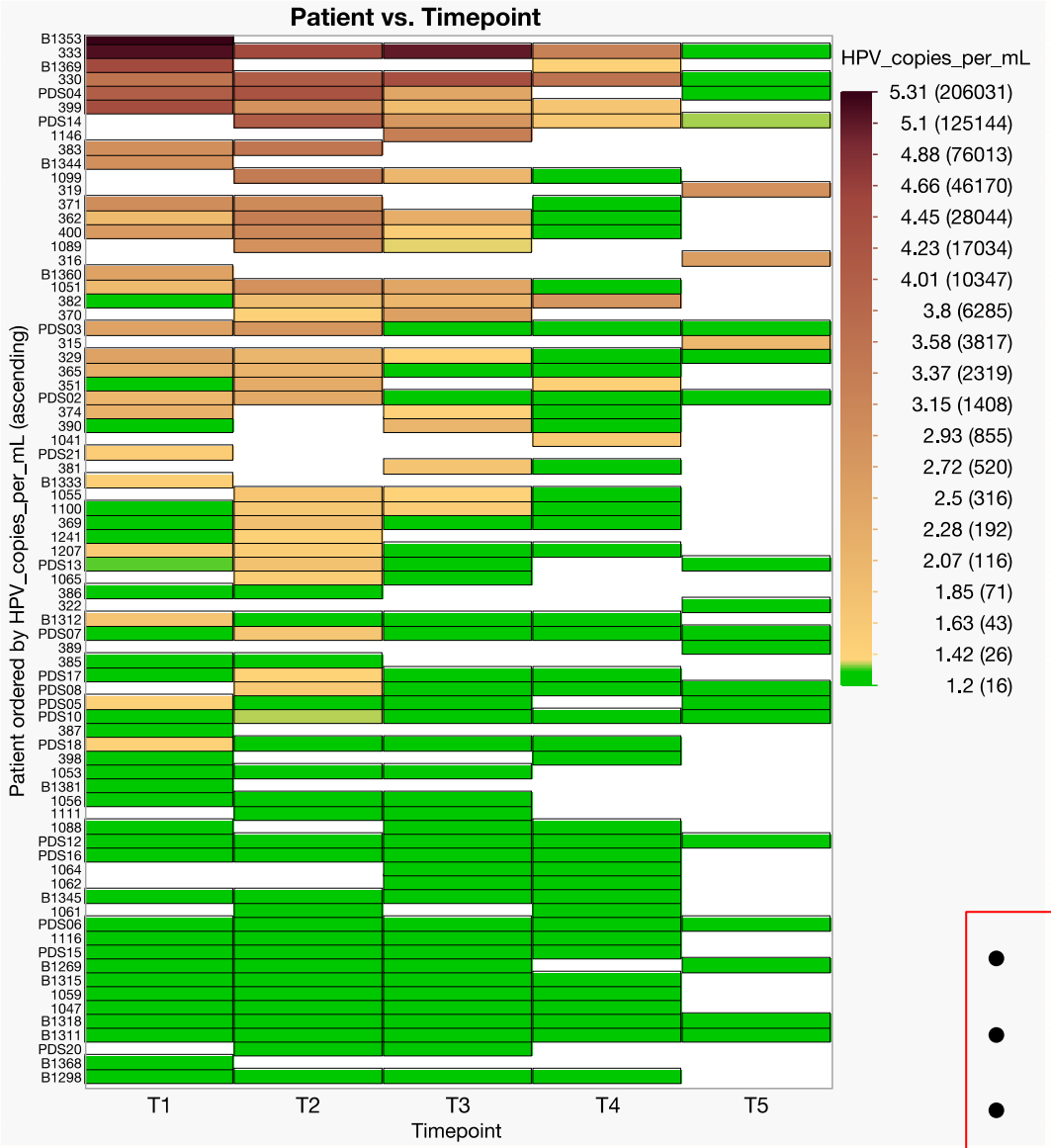
# Peak Timepoints

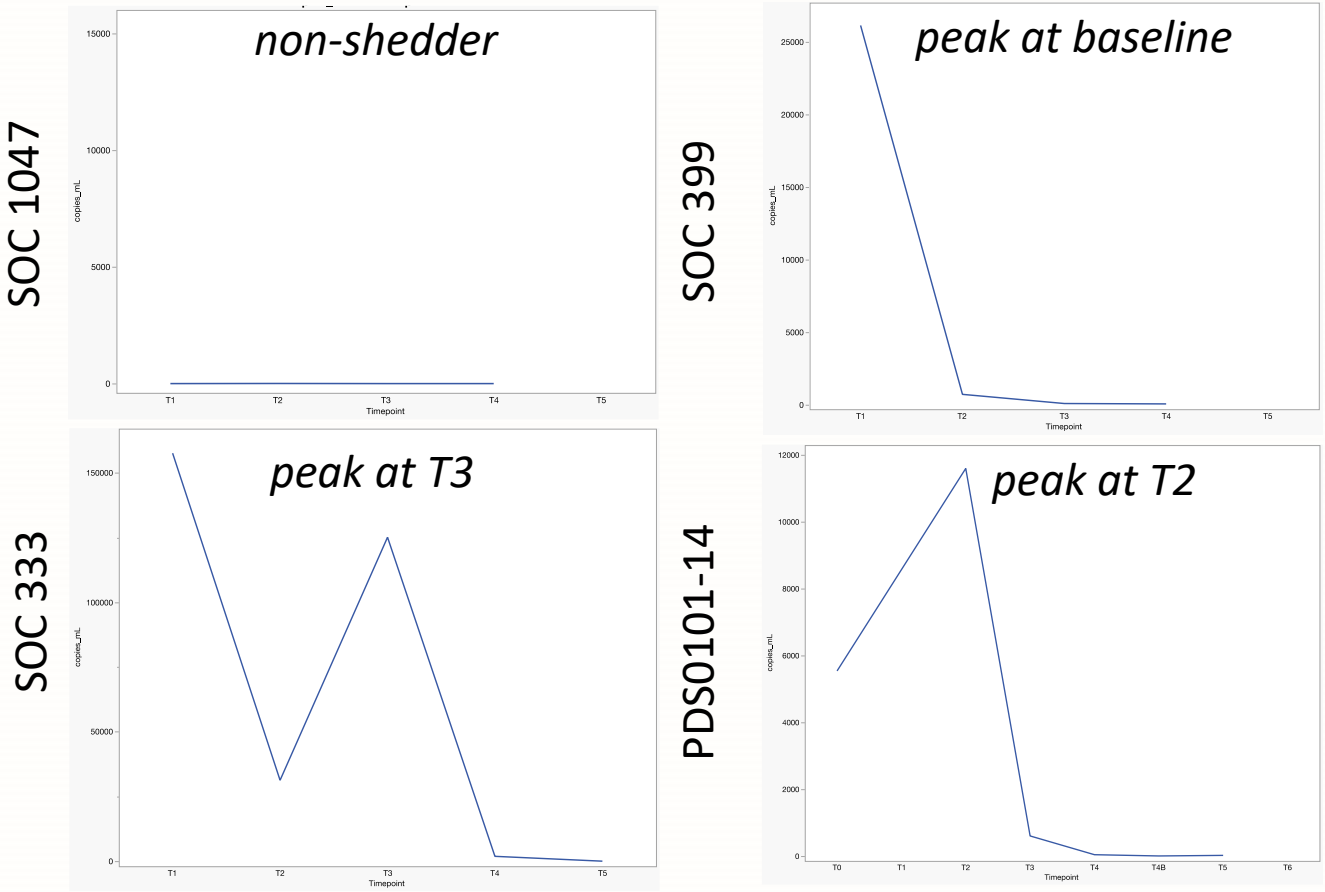
at least 3 measurements




53% of pts peak during week 1 of EBRT

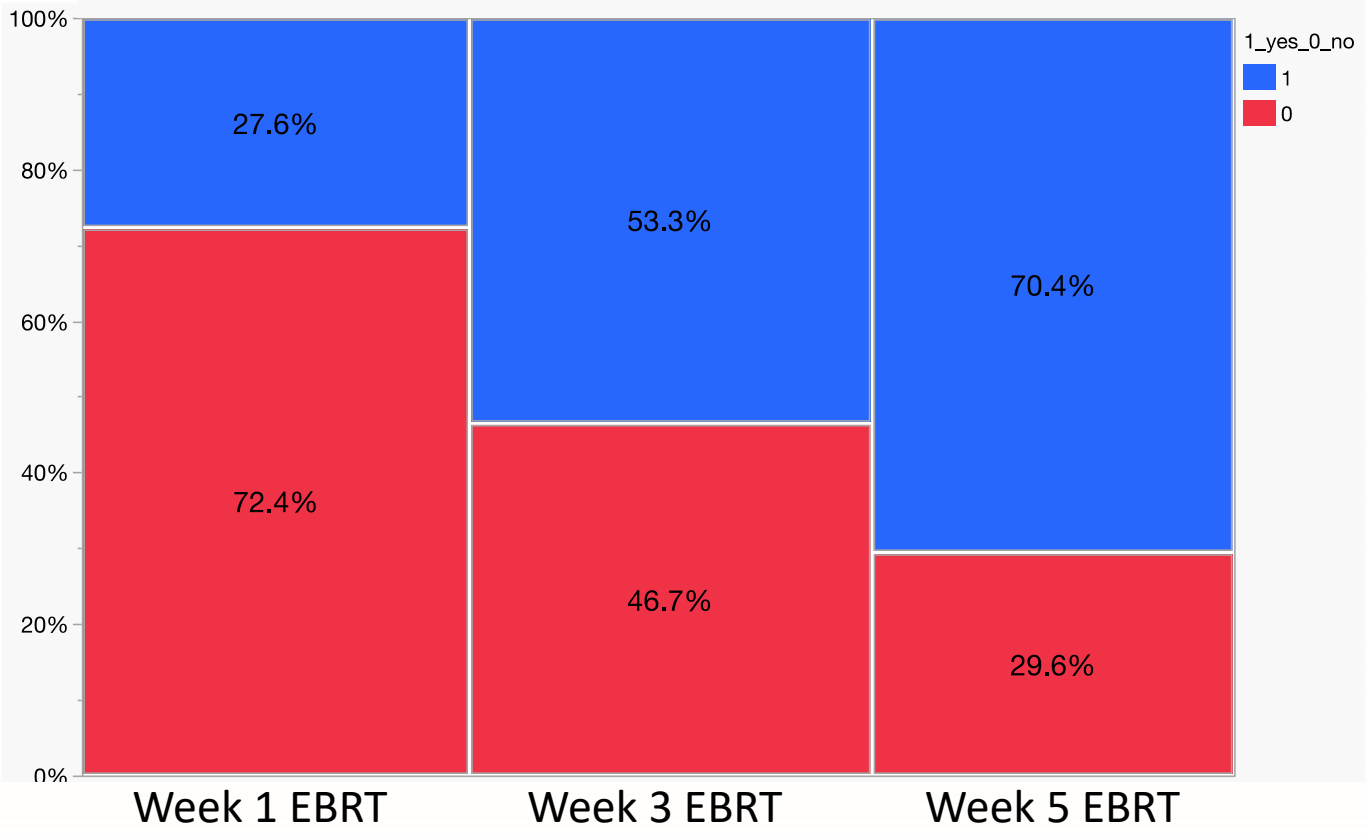
# cfDNA during and after RT

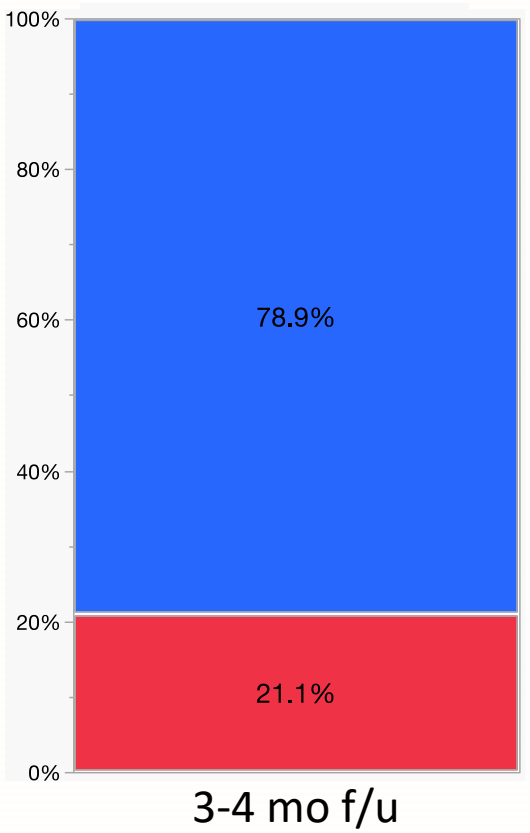



- Many cfDNA level trajectories
- Possible: Undetected at baseline → Detected later
- Pts w/ higher baseline levels: may take longer to clear

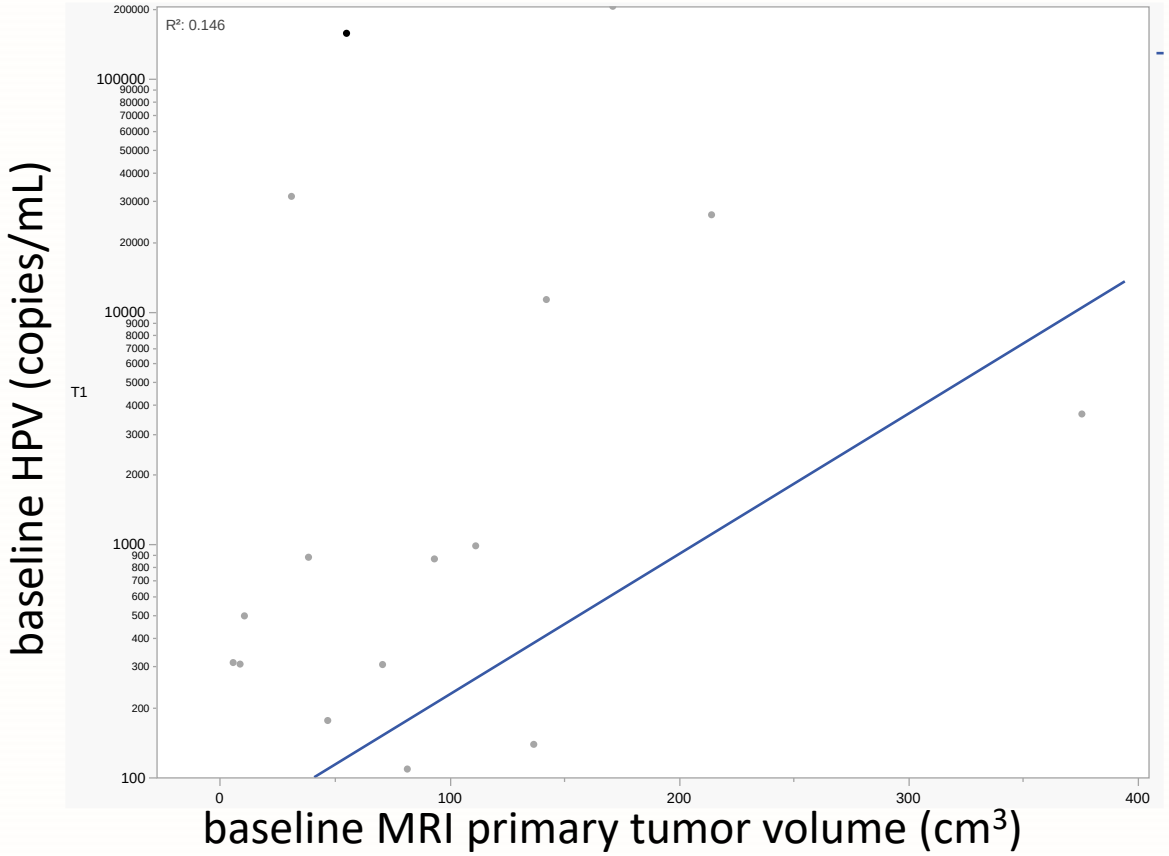
# cfDNA clearance during and after EBRT




- HPV cfDNA clearance progressively increases throughout EBRT
- 70.4% of pts cleared during week 5 of EBRT; 78.9% at 3-4 mo f/u

# Baseline cfDNA & Tumor Volume

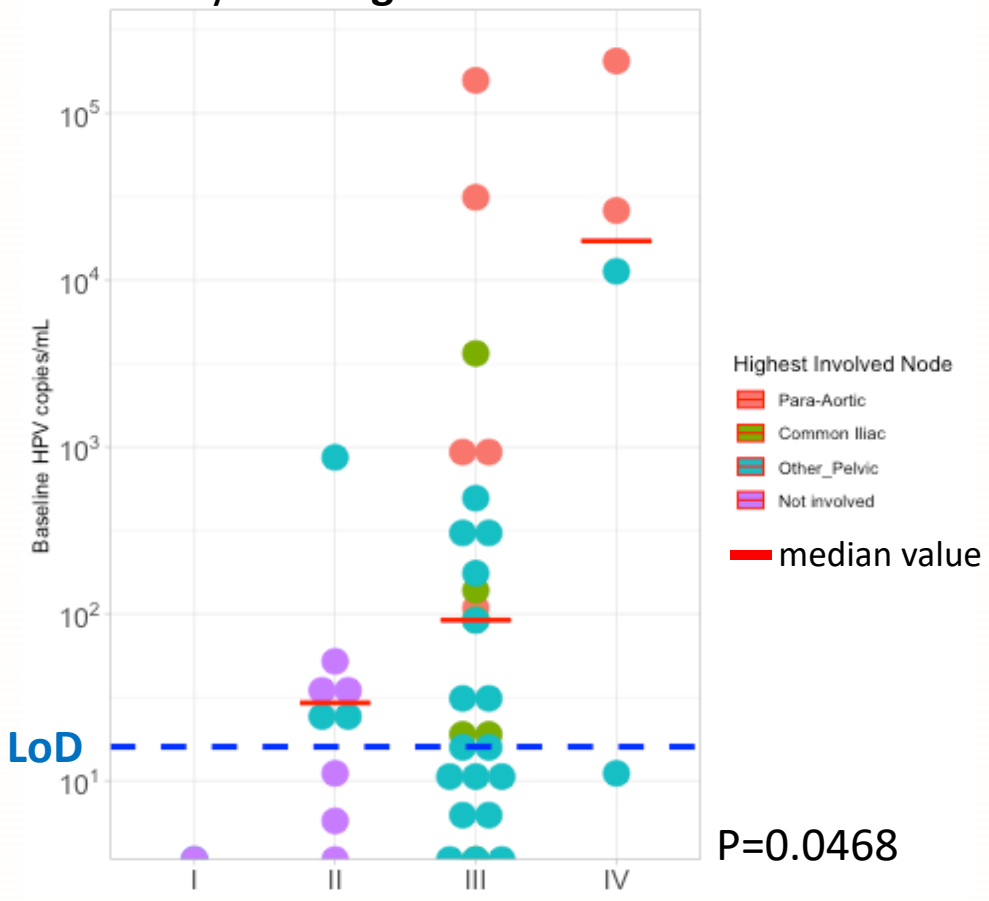



$\rho$ = 0.249
p = 0.103

No clear association between baseline HPV cfDNA level and primary tumor volume

# Baseline cfDNA & FIGO Stage, Nodal Involvement

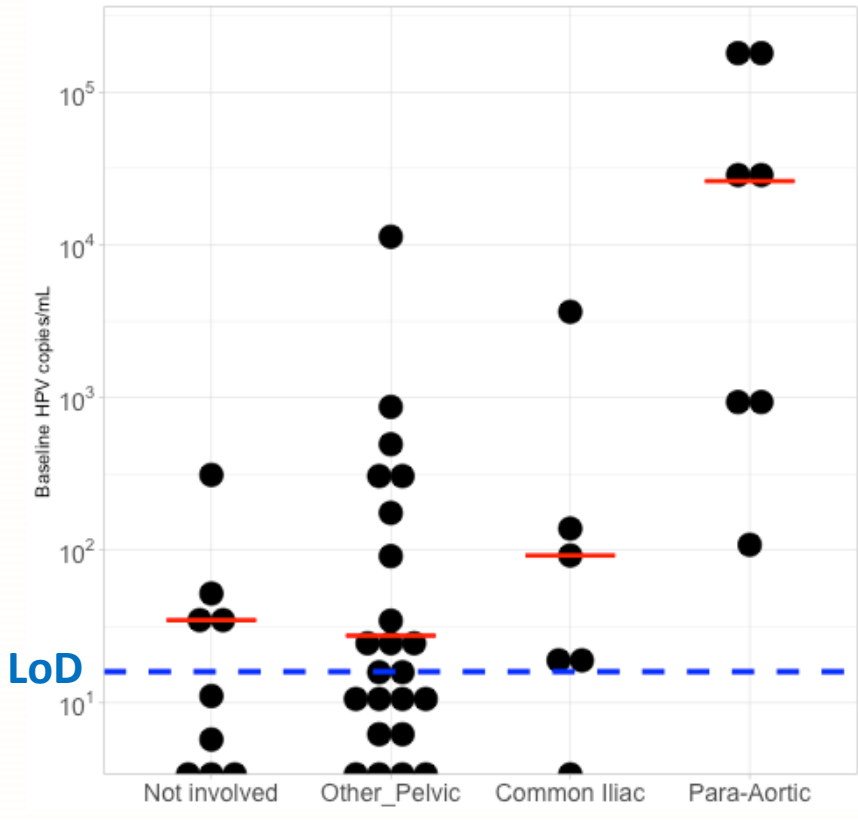
Baseline HPV cfDNA levels by: **Stage**




P=0.0468

HPV cfDNA level associated with FIGO 2018 Stage

**Highest Involved Node**

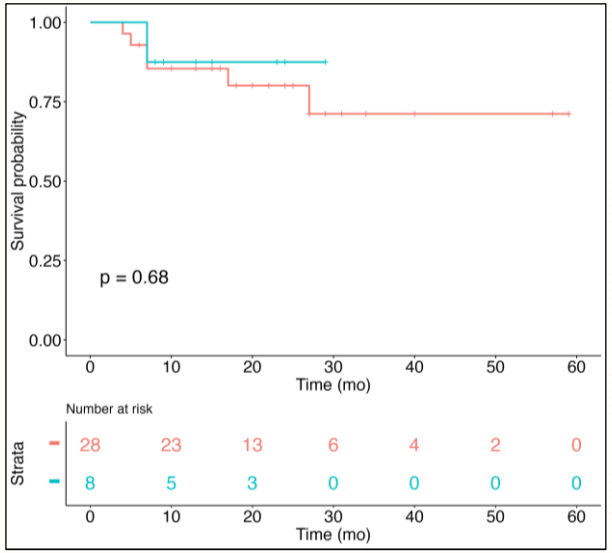



P=0.0016

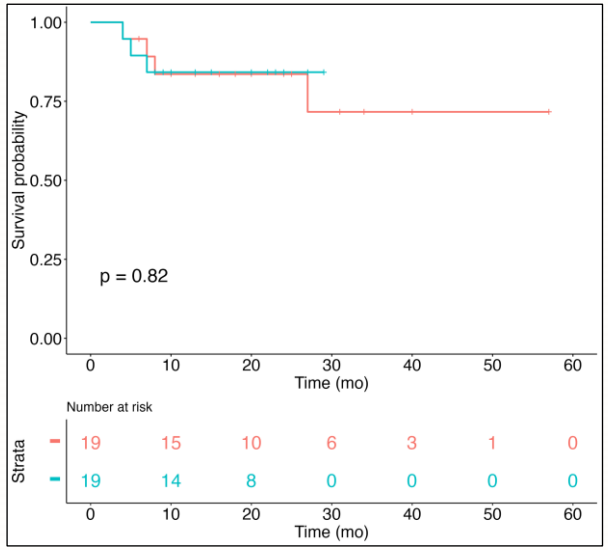
HPV cfDNA level associated with para-aortic nodal involvement

# Clearance at Timepoint & Recurrence-Free Survival (RFS)

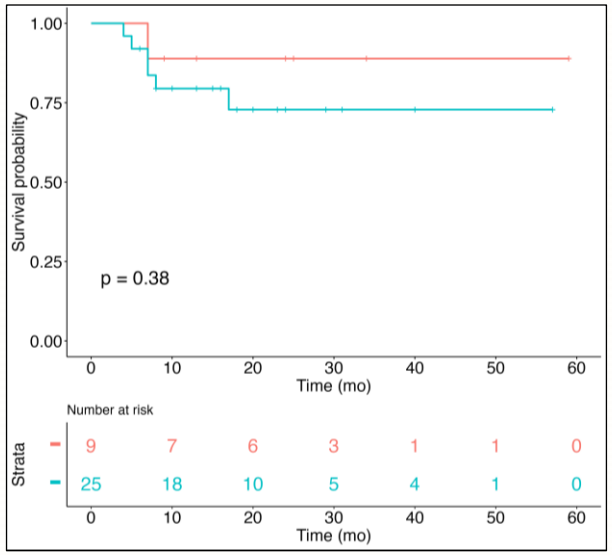
**During Week 1 EBRT**



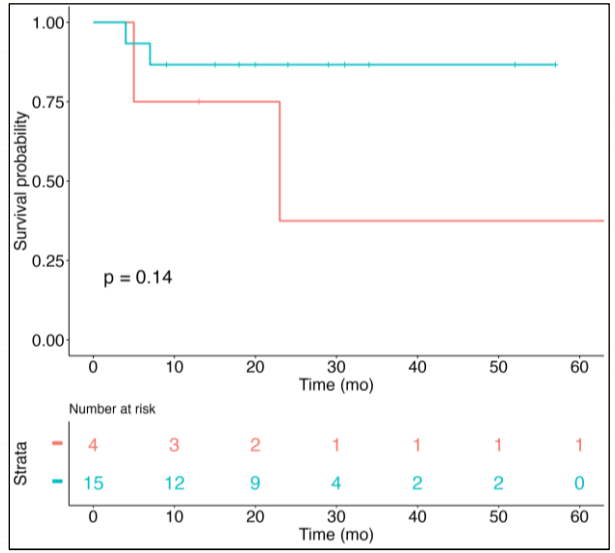

**During Week 3 EBRT**

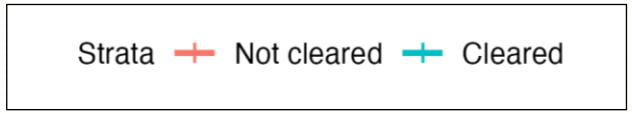



**During Week 5 EBRT**




**3-4 mo f/u**



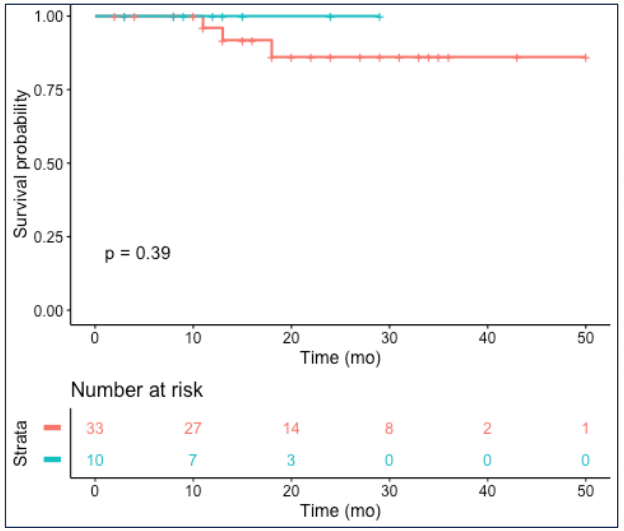




pooled median f/u: 24 mo

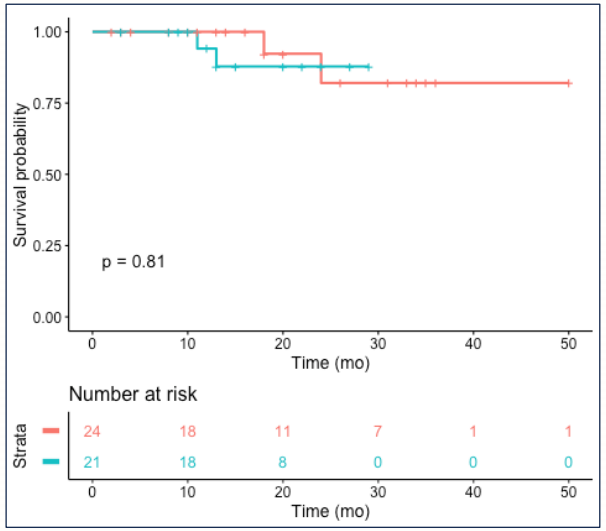
- Early analysis: no clear association b/w timing of HPV cfDNA clearance during EBRT & RFS
- Limited # of “HPV cfDNA not cleared” f/u samples, but these pts potentially have worse RFS

# Clearance at Timepoint & Overall Survival

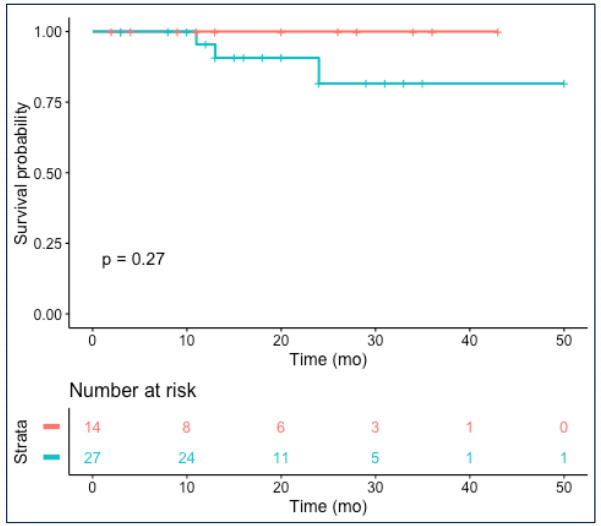
### During Week 1 EBRT



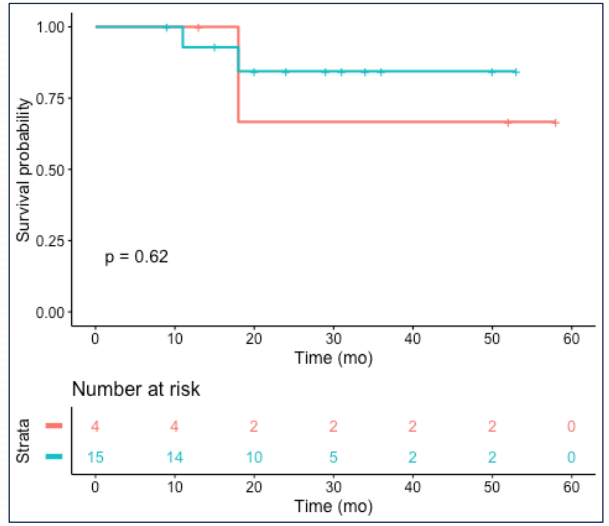

### During Week 3 EBRT




### During Week 5 EBRT




### 3-4 mo f/u



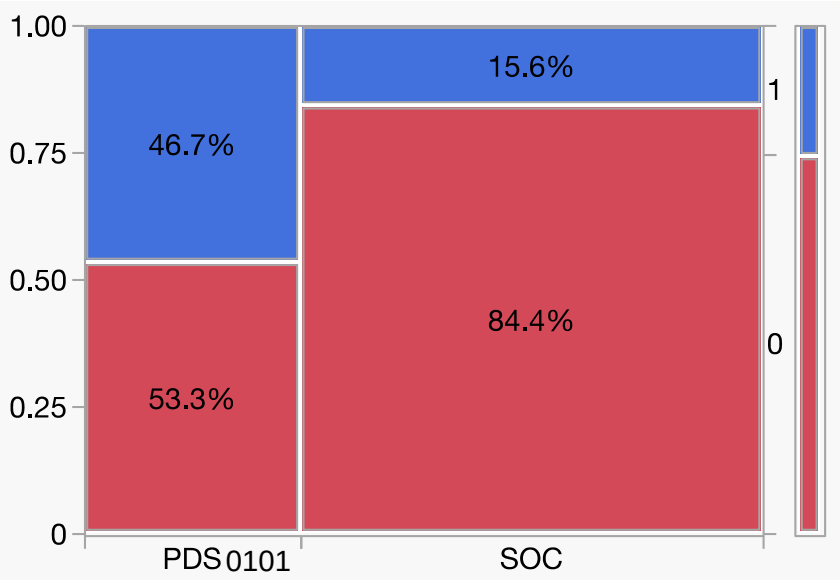

pooled median f/u: 26 mo

Strata Not cleared Cleared

Similar story to RFS: no clear associations in early analysis, will need longer f/u data

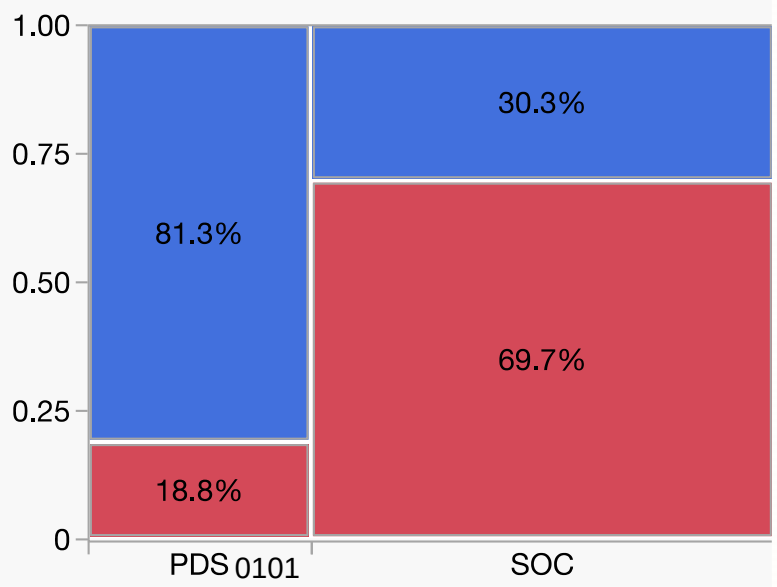
# PDS0101 vs SOC: cfDNA Clearance Timepoints

**Clearance after 1 week EBRT (T2)**



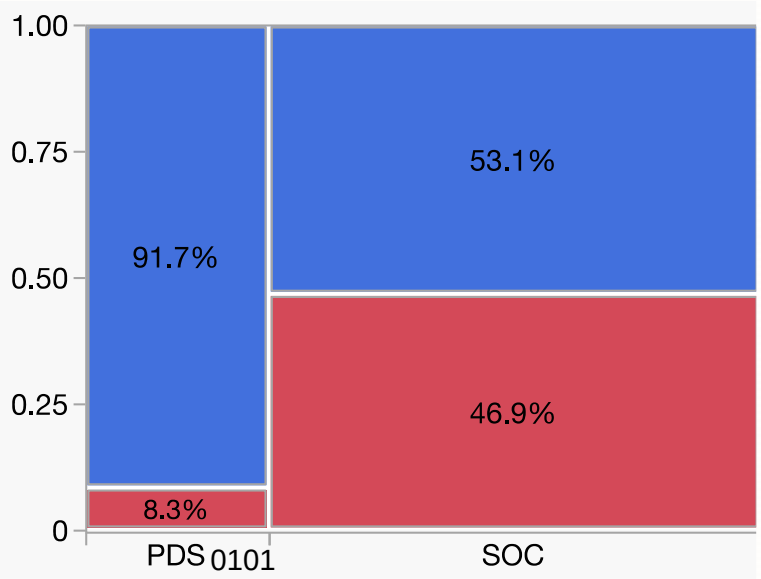

P=0.0341

**Clearance after 3 weeks EBRT (T3)**




P=0.0018

**Clearance after 5 weeks EBRT (T4)**

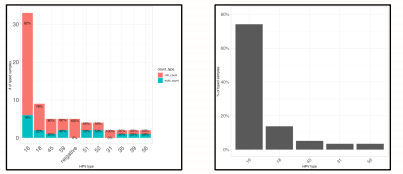
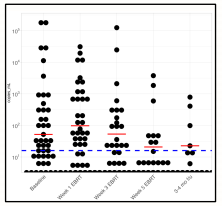
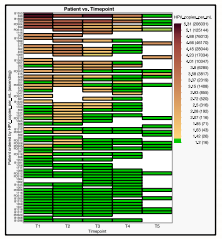
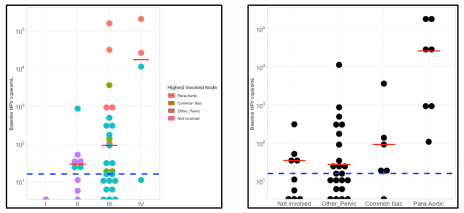
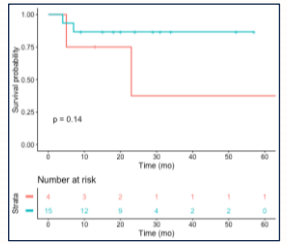



P=0.0179

Earlier and greater proportion of cfDNA clearance in PDS0101 compared to SOC

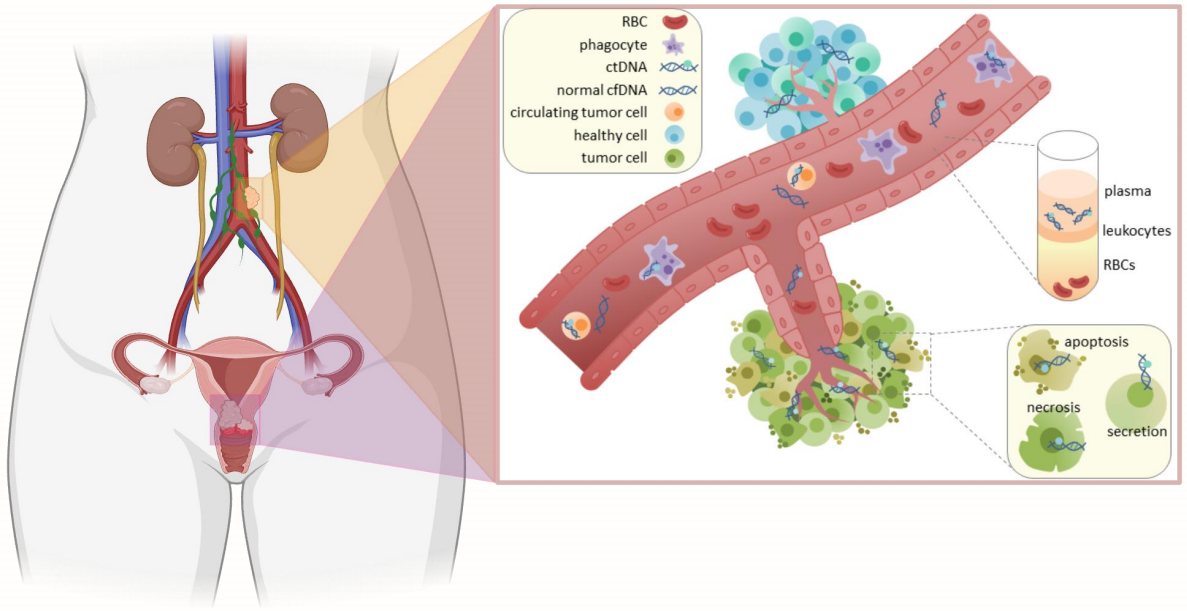
# Conclusions

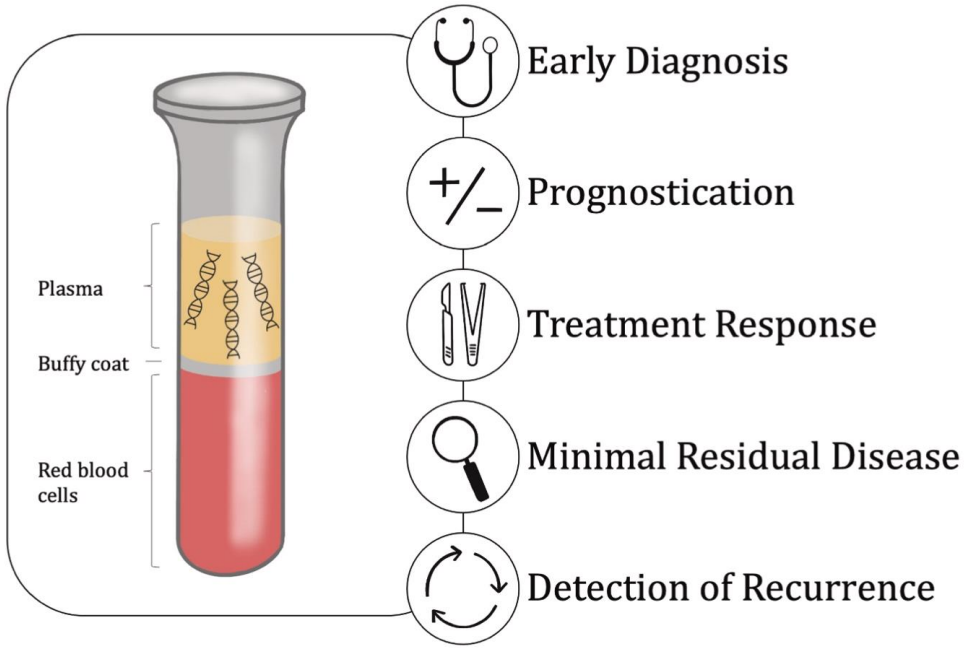
- Tumor HPV- ≠ cfDNA HPV-
- Wide range of HPV cfDNA levels
- HPV cfDNA levels generally peak during EBRT, and many pts clear HPV cfDNA by end of EBRT
- HPV cfDNA levels associated w/ stage & nodal level involvement
- No clear associations with survival outcomes in early analysis

# Future Directions, Considerations

- Continue sample collection, data analysis
- Compare with additional imaging & molecular correlative data
- Role for poor ctDNA clearance or f/u ctDNA detectability to guide ”outback” chemo?




Haring *Oral Oncology* 2022

# Acknowledgements


**Our patients**

**Klopp Lab**

Ann Klopp

Tatiana Cisneros Napravnik

Kyoko Court

Olsi Gjyshi

**Gillison Lab**

Maura Gillison

Weihong Xiao

**Gyn Rad Onc Research**

Erica Lynn  Julie Sammouri

**Gyn Rad Onc Clinical Service**

Lauren Colbert  Patricia Eifel

Anuja Jhingran  Melissa Joyner

Lilie Lin

**Diagnostic Radiology**

Aradhana Venkatesan

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