Plasma Circulating Tumor HPV DNA for the Surveillance of Cancer Recurrence in HPV-associated Oropharyngeal Cancer

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Disclosure for Dr. Chera

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Background

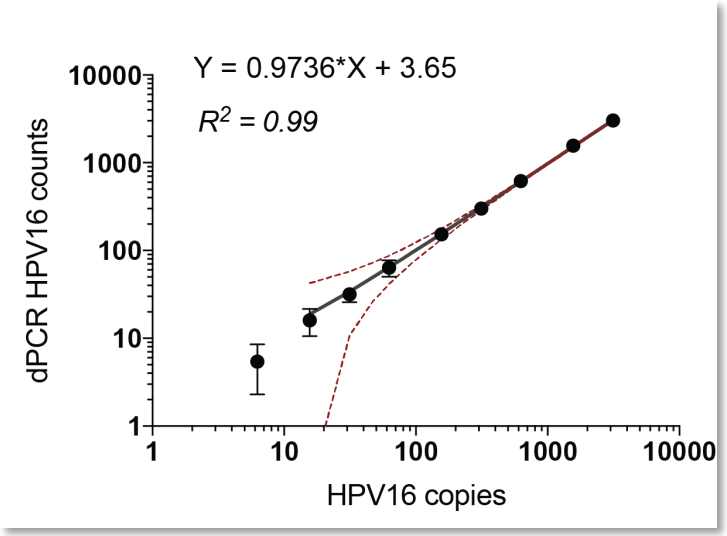
- Plasma circulating tumor HPV DNA (ctHPVDNA) is detected in a majority of HPV-OPSCC patients

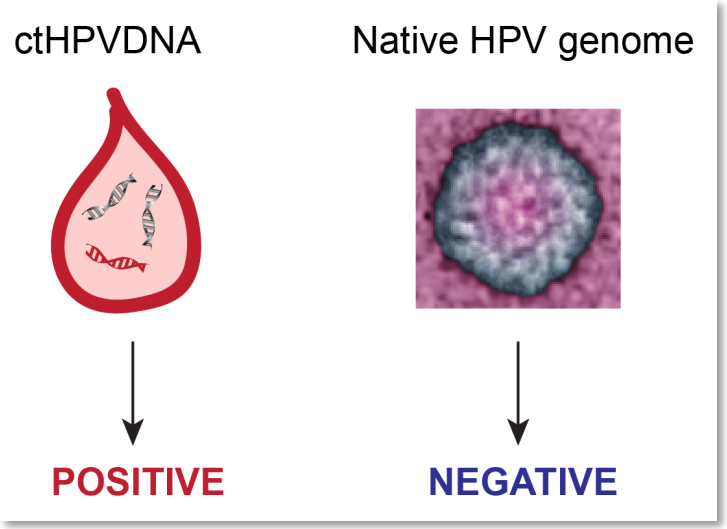
- Potential biomarker of tumor burden and response kinetics

- *Can plasma ctHPVDNA be used to detect cancer recurrence?*

Cao H, …, Le QT, *IJROBP* 2012
Wang Y, …, Agrawal N *Sci Transl Med* 2015
Chera B, …, Gupta G *ASTRO* 2017
Gupta G, …, Chera B *ASTRO/ASCO* 2018

Multi-analyte Digital PCR (dPCR) Assay for ctHPVDNA



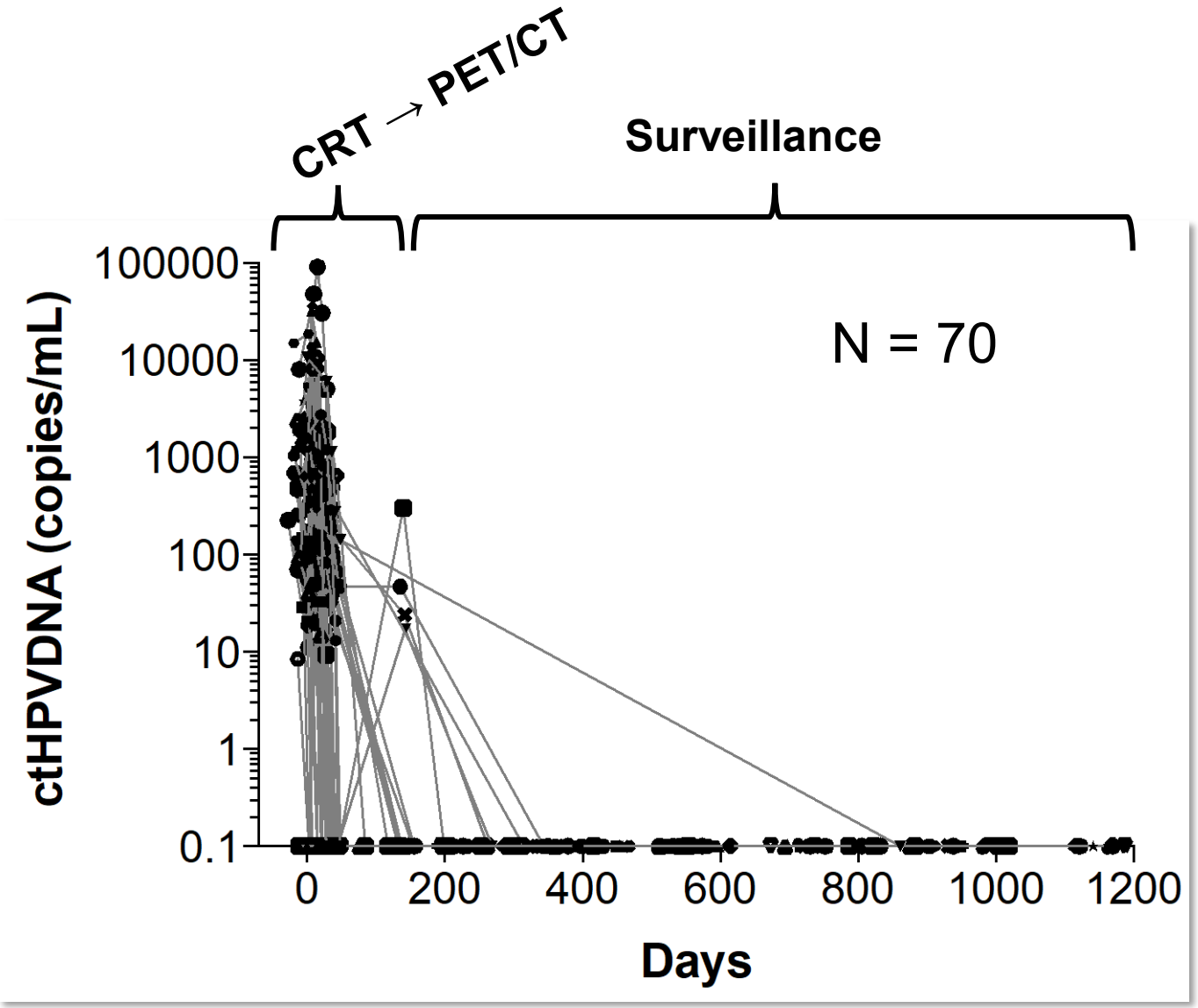


- Standardized multi-step analytical protocol to optimize specificity and sensitivity
- Distinguishes ctHPVDNA from native viral genomes
- Detects ctHPV-16, -18 ,-31, -33, and -35 (more high-risk strains coming)

Chera B, …, Gupta G *ASTRO* 2017
Gupta G, …, Chera B *ASTRO/ASCO* 2018

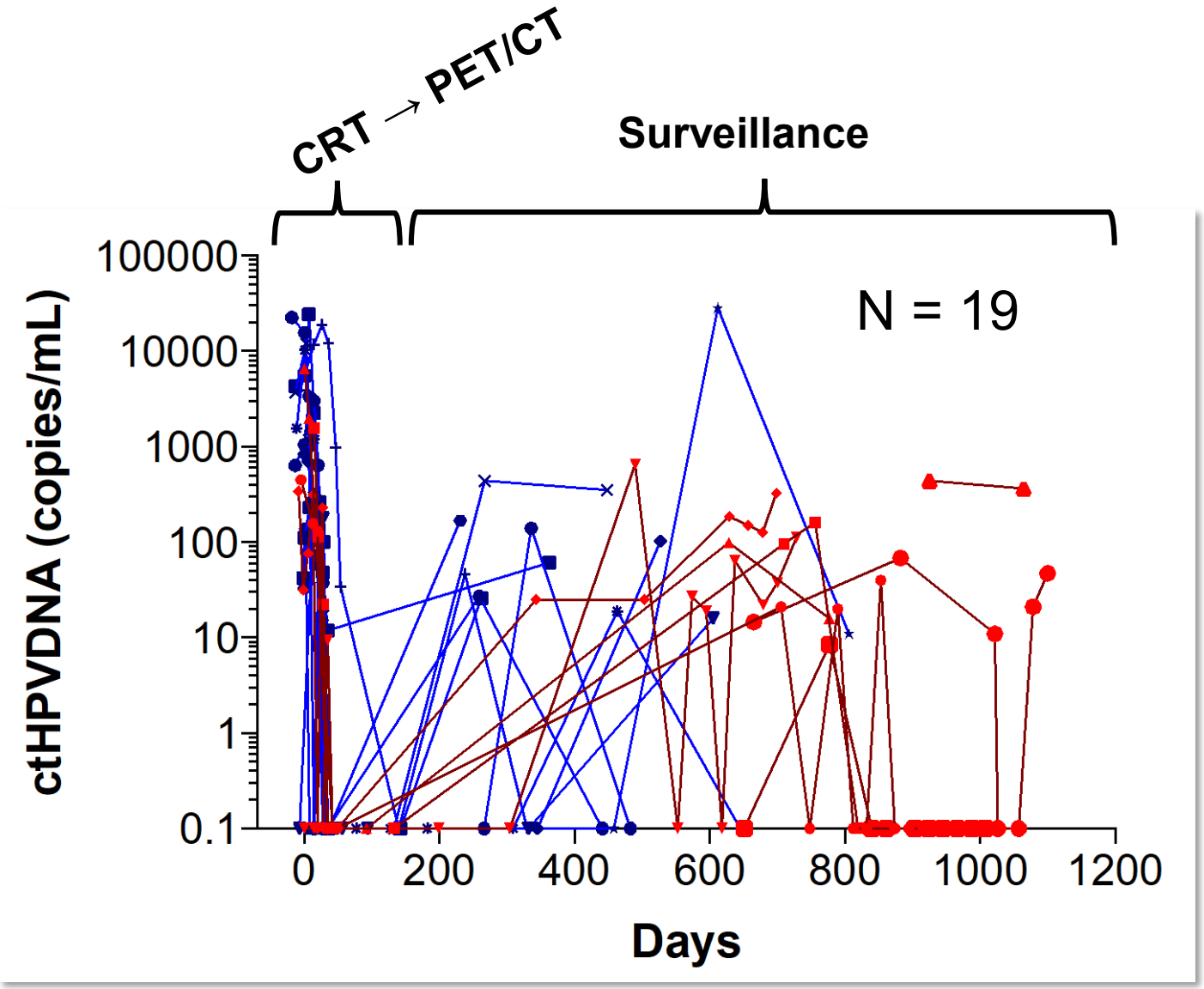
Method: Prospective Biomarker Trial

- 89 patients with biopsy-proven HPV-associated OPSCC
- All patients received definitive chemoradiation
- Blood specimen collection/analysis *(~1000 blood samples)*
  - 58/89 had pretreatment assessment (65%)
  - 89/89 had surveillance/posttreatment assessments (100%)
- Clinical surveillance
  - Every 2 - 4 months for years 1 - 2, every 6 months for years 3 – 5
  - Chest imaging every 6 months
  - Additional imaging was obtained if ctHPVDNA became detectable
- Events were defined as recurrence after the 3 month post-CRT PET/CT



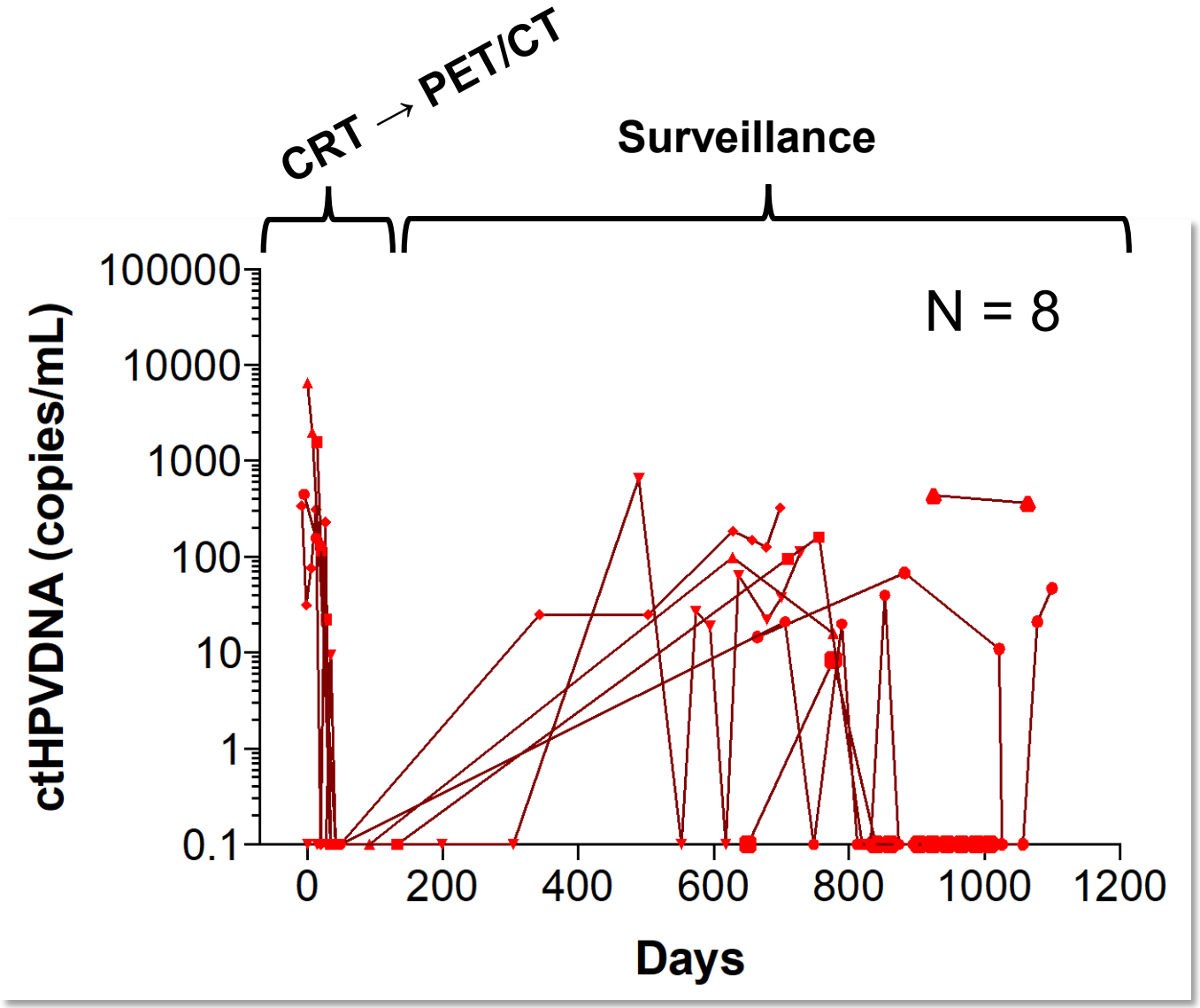
Undetectable ctHPVDNA

- 70 out of 89 patients (79%) had undetectable ctHPVDNA during surveillance
- All 70 of these patients remain disease free (**NPV = 100%**)



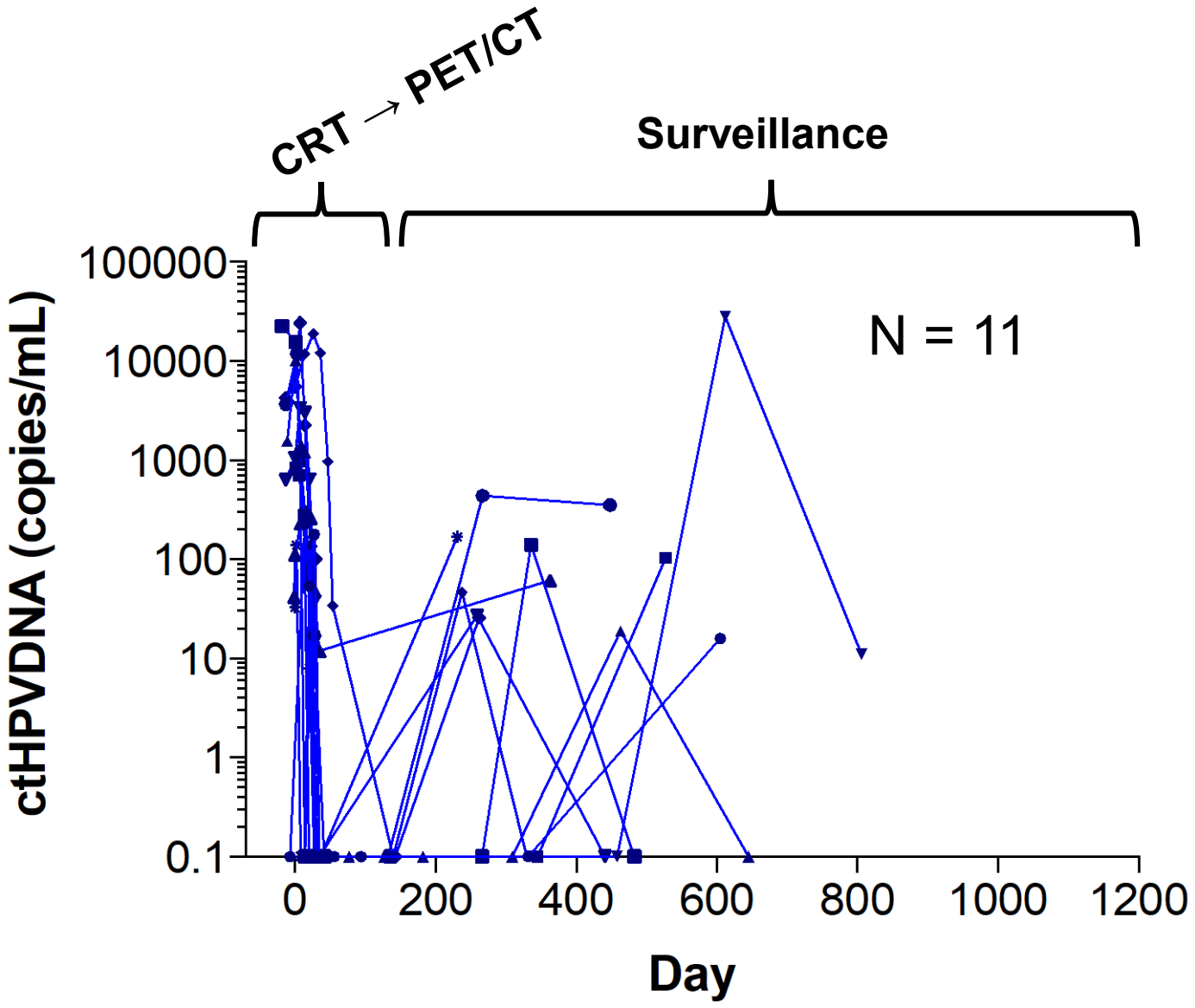
Detectable ctHPVDNA

- 19 out of 89 patients (21%) had a positive ctHPVDNA signal at one or more followup timepoints
- 8 out of these 19 patients have developed biopsy-proven recurrence (**PPV = 42%**)
- **P < 0.0001** (two-tailed Fisher's exact test)



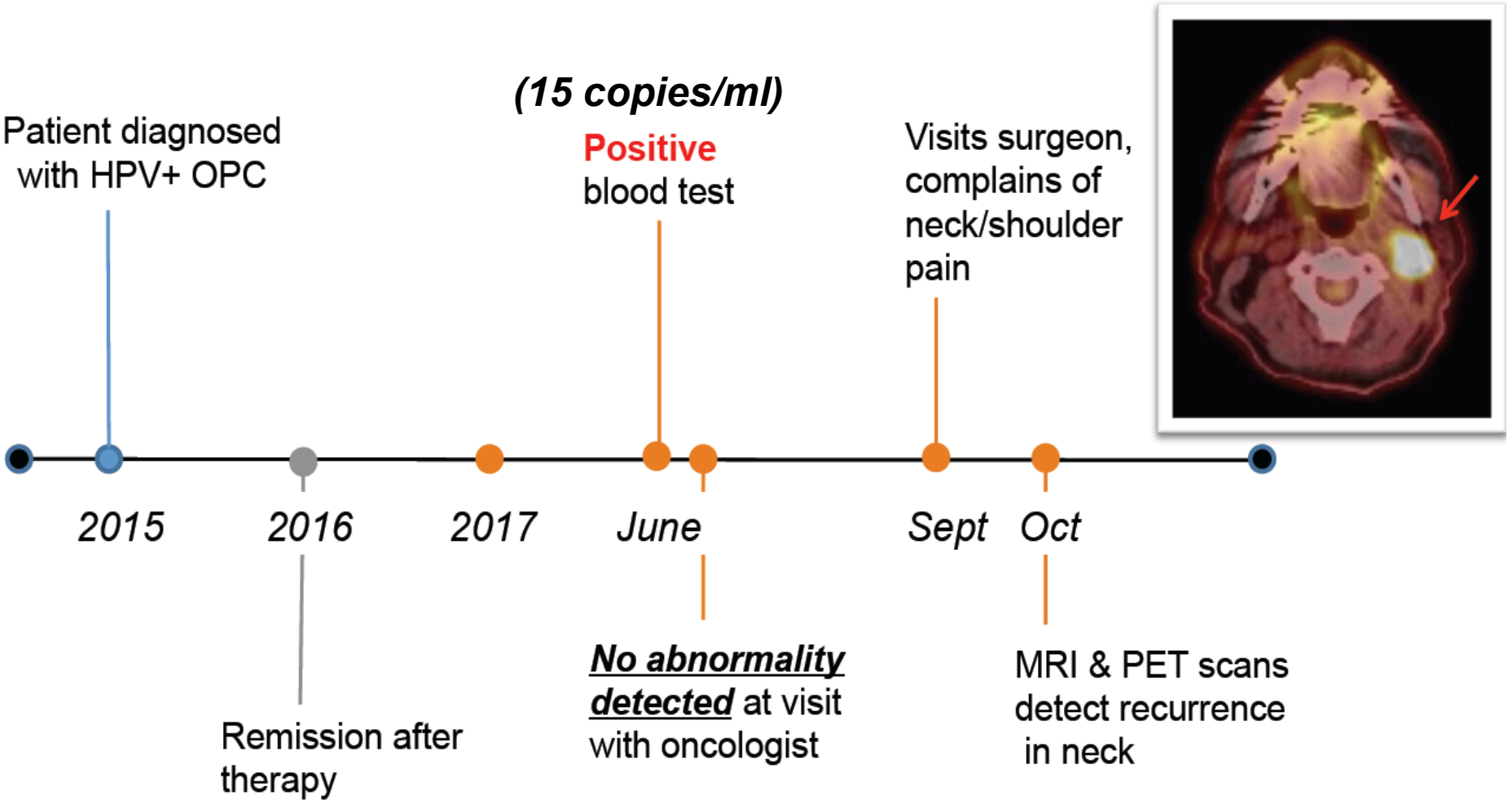
Detectable ctHPVDNA *with* Recurrence

- 8 patients with biopsy-proven recurrence:
  - ➤ 0 local
  - ➤ 1 regional only
  - ➤ 3 regional and distant
  - ➤ 4 with distant
- All patients remain alive
- 3 patients are currently NED by imaging and blood tests (2 patients on immunotx, 1 post-chemo)

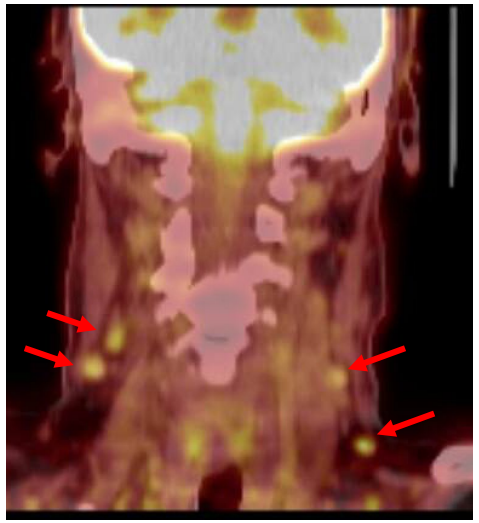


Detectable ctHPVDNA *without* Recurrence

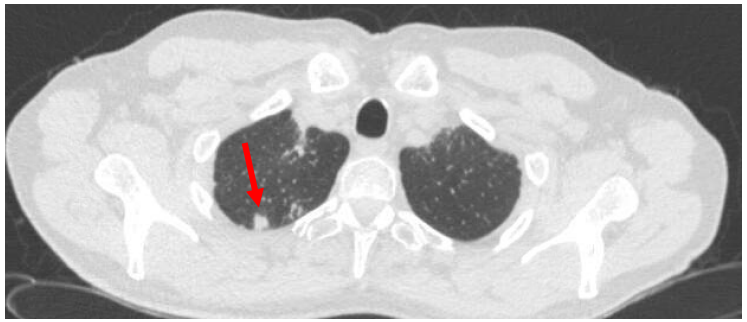
- 11 patients had detectable ctHPVDNA but no recurrent disease evident on imaging
- 4 patients spontaneously cleared their ctHPVDNA signal → *immune effects?*
- The remaining 7 patients continue to be closely monitored

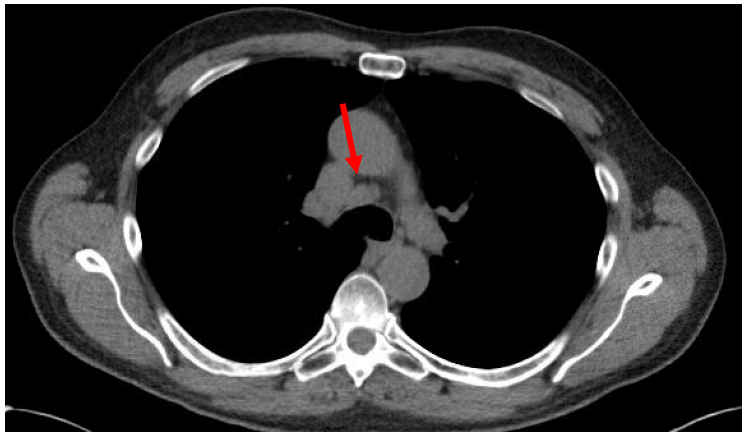

(15 copies/ml)
Positive
blood test
Patient diagnosed
with HPV+ OPC
Visits surgeon,
complains of
neck/shoulder
pain
2015
2016
2017
June
Sept
Oct
Remission after
therapy
No abnormality
detected at visit
with oncologist
MRI & PET scans
detect recurrence
in neck

3 month post-CRT
0/27 nodes positive
0 copies/ml



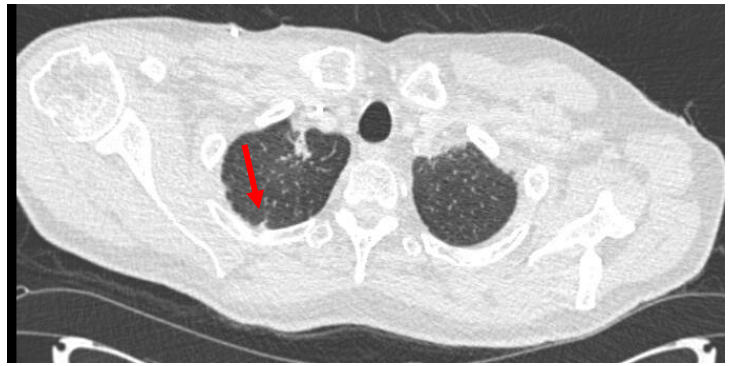
22 months post-CRT
96 copies/ml

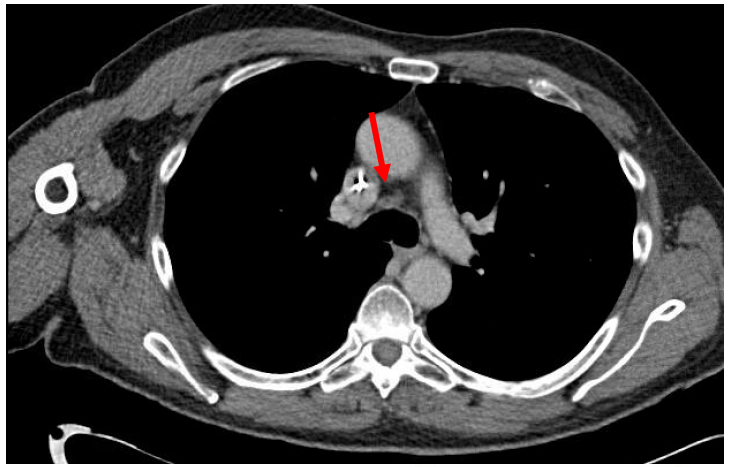




PET/CT
Bronch & FNA
6 weeks carbo/taxol

28 months post-CRT
0 copies/ml





Conclusions

- A multi-analyte ctHPVDNA assay detects patients at risk of cancer recurrence
- None of the patients with undetectable ctHPVDNA during post-treatment surveillance developed disease recurrence (NPV = 100%, N=70).

Future Directions:

- Limit cross-sectional imaging to patients who are at greatest risk → reduced cost and radiation exposure
- Early detection may increase effectiveness of salvage therapy
- Possibility of more frequent monitoring
- Possible avoidance of invasive biopsy procedures for patients with radiographic correlate and detectable ctHPVDNA