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Clinical Validation of HPV ctDNA for Early Detection of Residual Disease Following Chemoradiation in Cervical Cancer

Presented by:

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Disclosure & Study Team

- Employer: Princess Margaret Cancer Centre, University of Toronto
- Advisory Board: AstraZeneca
- Patent: HPV ctDNA (HPV seq) pending
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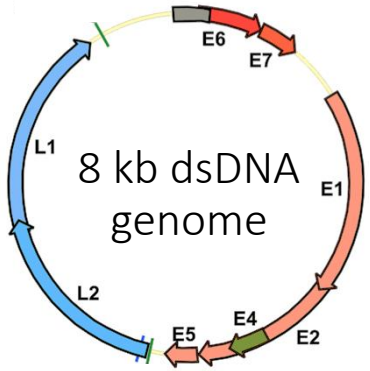
Background

- Tumours continually shed their DNA into the circulation
- Majority (>90%) of cervical cancer caused by human papillomavirus (HPV)
- Non-invasive liquid biopsy tests can detect HPV circulating tumor DNA (ctDNA) in the blood as a measure of disease burden
- Our pilot study showed detectable HPV ctDNA at the end of chemoradiation is associated with worse progression-free survival

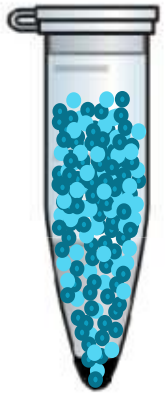
HPV



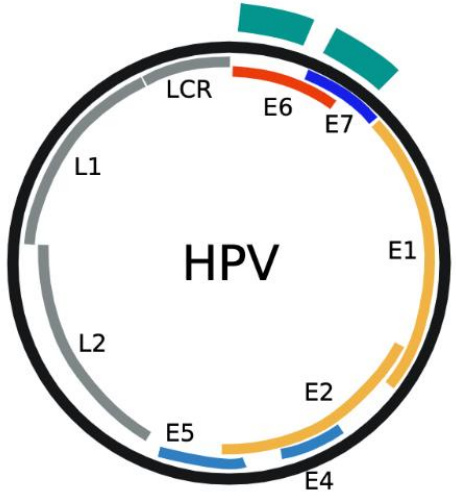
Han et al, JCO Prec Oncol, 2018; 2:1-8
Leung, Han*, et al. Clin Cancer Res 2021; 5857-68*

Newer HPV ctDNA detection technologies

(A) Droplet-based digital polymerase chain reaction (dPCR)

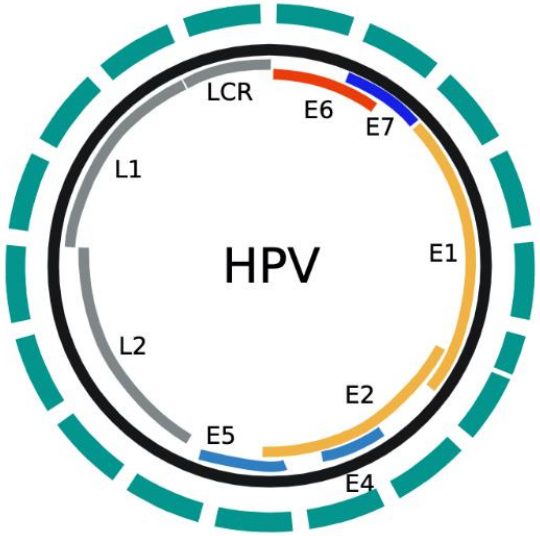


Sample partitioned into thousands of nanoliter-sized droplets, each with independent amplification events



dPCR probes target <u>E6 & E7</u> regions

(B) Next generation sequencing (HPV-seq)

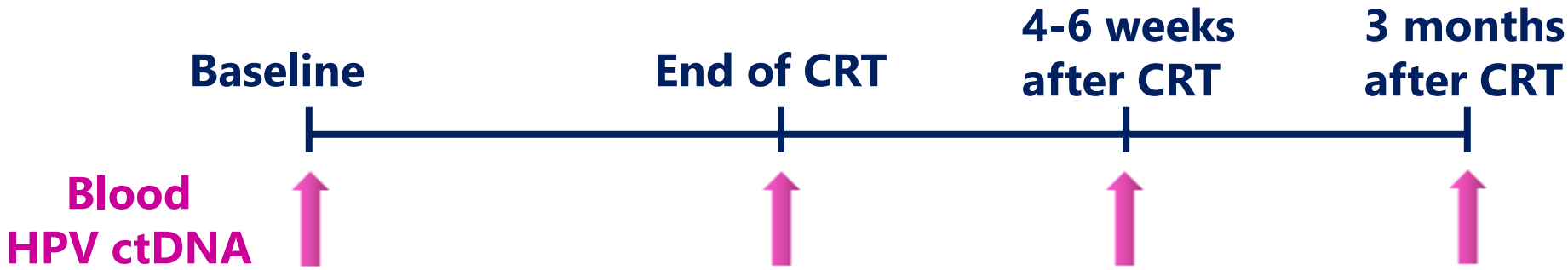


Probes tiling the entire genome allow <u>full coverage</u> of HPV

Rostami, Bratman, Han. Clin Cancer Res 2021; 5158-60

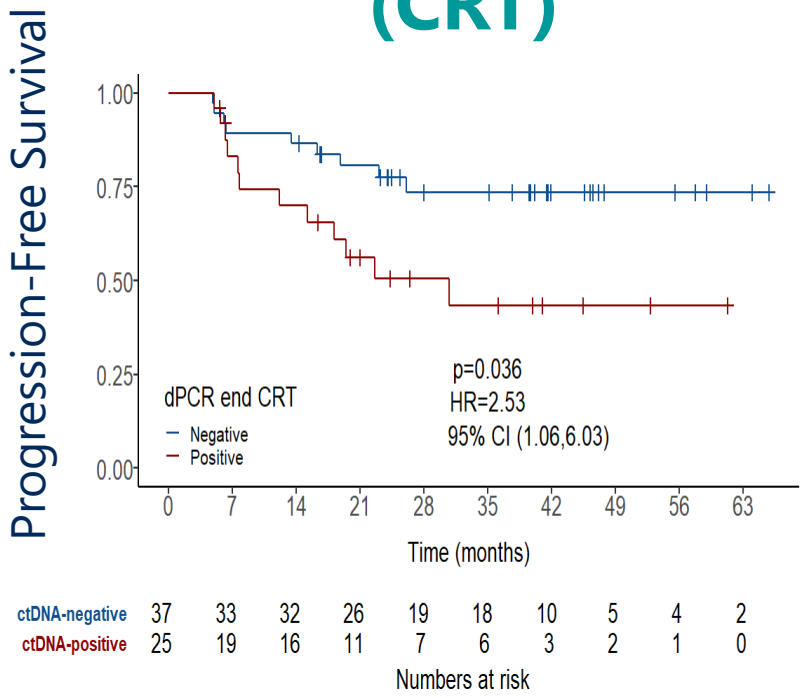
Method

- Prospective multicenter validation study
- 70 patients with stage IB-IVA HPV+ cervical cancer treated with definitive (chemo)radiation between 2017-2022
- HPV genotype determined using baseline plasma sample with HPV-seq
- HPV genotype-specific plasma DNA levels quantified using dPCR & HPV-seq

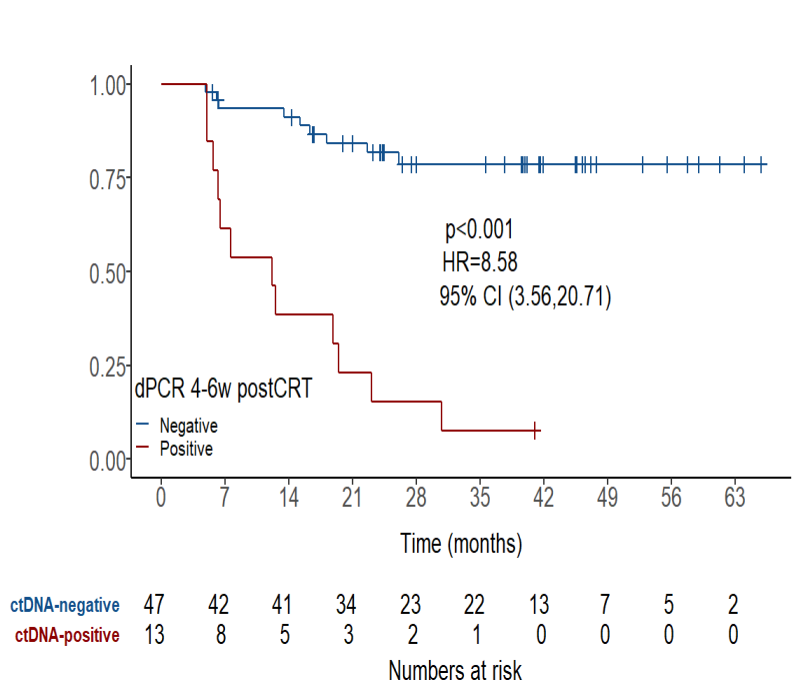


Results: dPCR

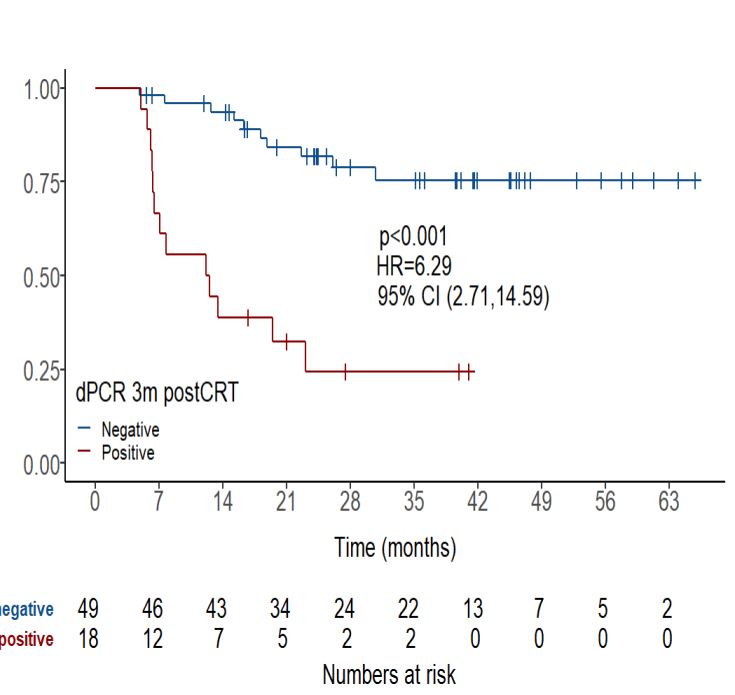
End of chemoradiation (CRT)



4 – 6 weeks post CRT



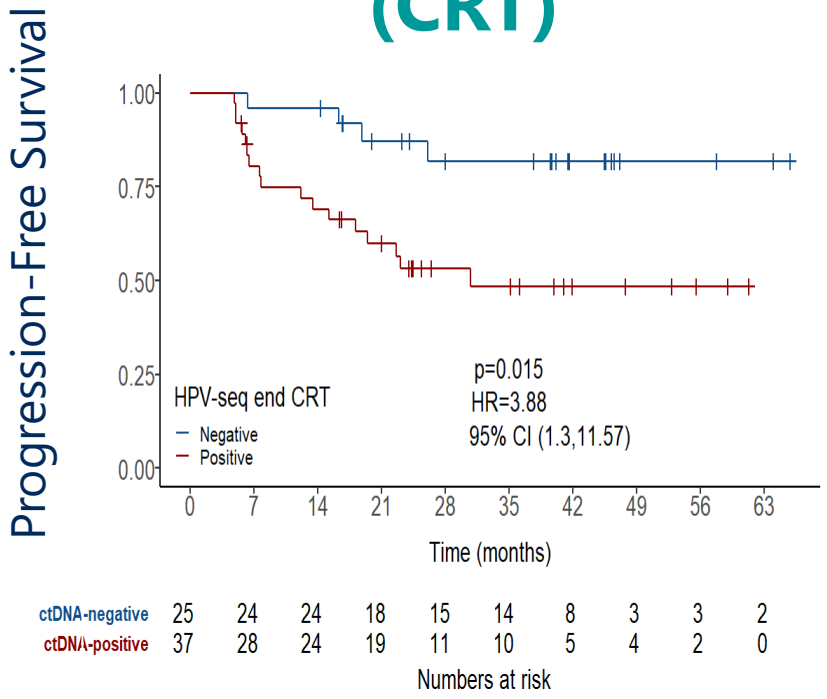
3 months post CRT



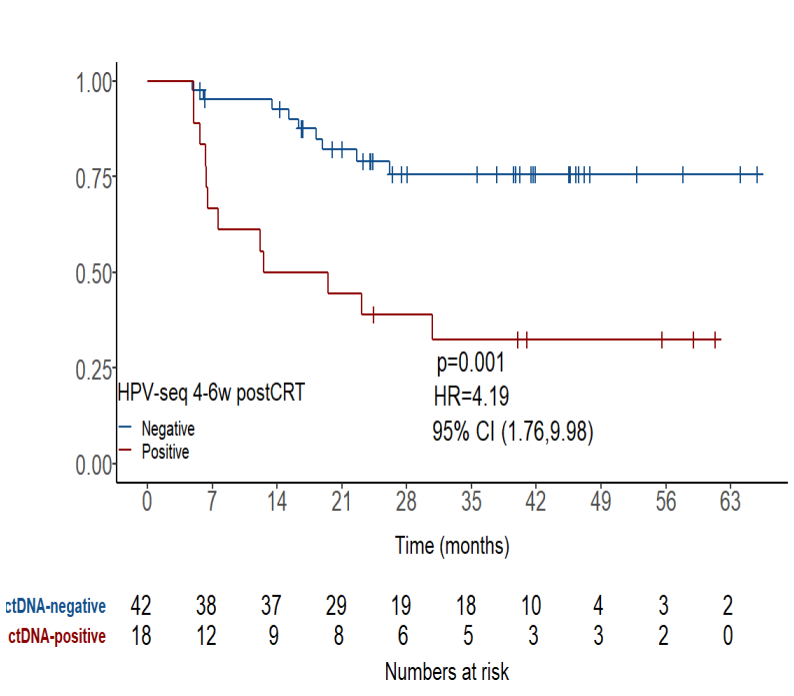
Undetectable HPV ctDNA — Detectable HPV ctDNA

Results: HPV-seq

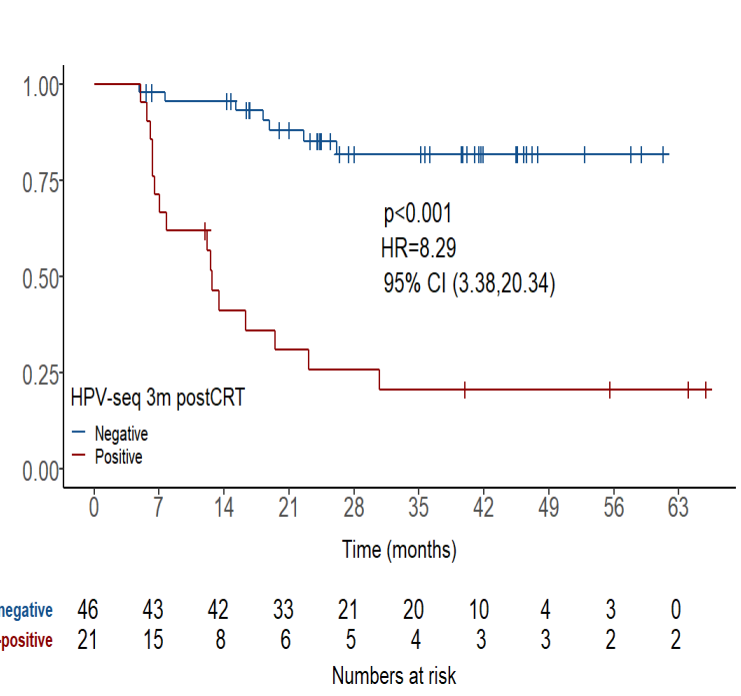
End of chemoradiation (CRT)



4 – 6 weeks post CRT



3 months post CRT



Undetectable HPV ctDNA Detectable HPV ctDNA

Conclusions

- HPV-seq enables determination of HPV type (genotyping) directly from plasma
- Persistent HPV ctDNA following chemoradiation is independently associated with inferior progression-free survival
- HPV ctDNA testing can be used to identify, as early as at the end of chemoradiation, patients at high risk of recurrence

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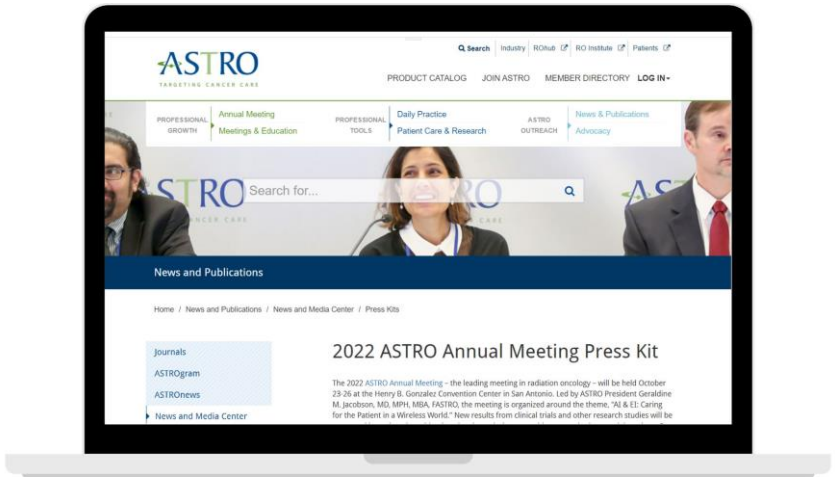

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