

# Prevalence of the HPV, EBV and TTV viral RNA in the plasma of patients with solid and hematologic neoplasms and the detection of a specific immune signature - Abstract # 2583



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## Background

EBV and HPV are considered human oncoviruses. In contrast, the torque teno virus (TTV) is not associated with any disease but its detection in circulation reflects the status of the immune system. TTV levels in peripheral blood plasma has been suggested as a tool for monitoring immunosuppressive therapy in patients post-allo-transplant.

## Methods

- Cell-free RNA (cf-RNA) extracted from plasma of 1139 cancer pts
  - 581 heme malignancy
  - 558 solid tumor
- NGS sequencing of all samples using targeted RNA panel including viral RNA of TTV, EBV, and HPV
  - Viral RNA testing selected to ensure only active and proliferating viruses detected
- Machine learning algorithm (random forest classifier) was trained and tested to explore immune/inflammatory biomarker expression profile differences between V+ cases (viral RNA positive) and V- cases.
  - Same model used to explore differences between TTV+, EBV+, and HPV+ cases

## Results

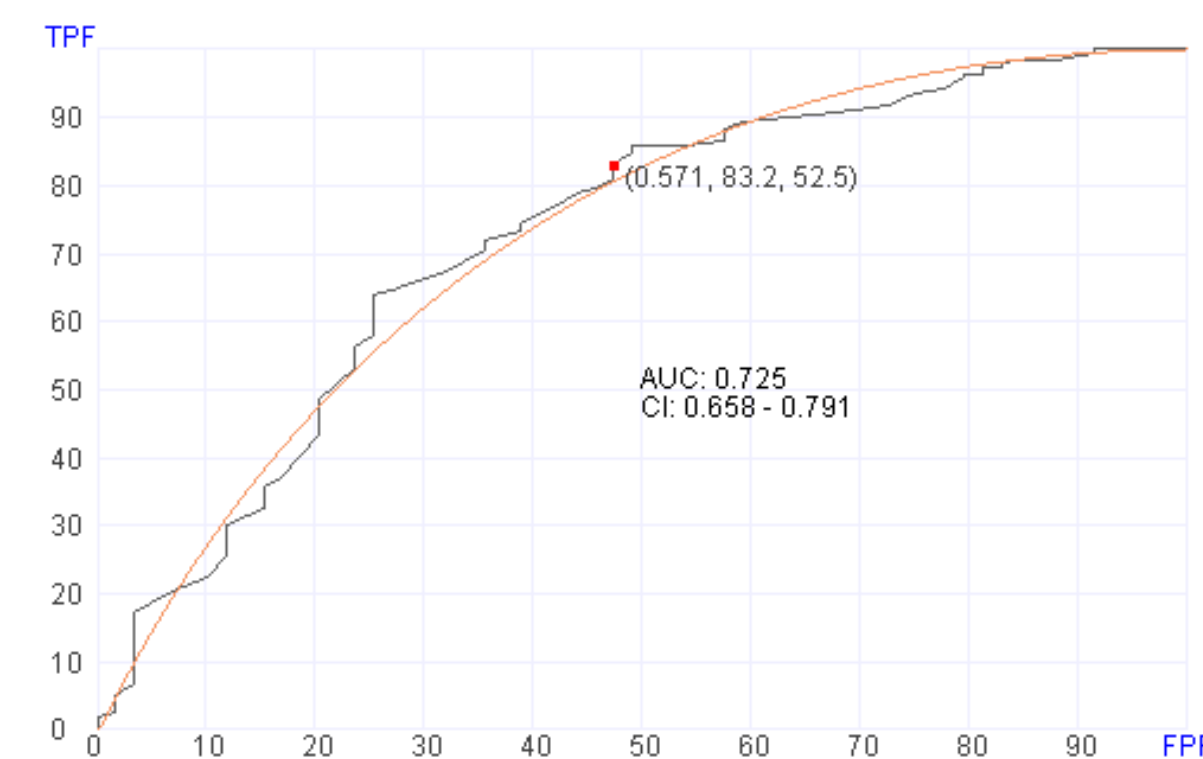
### Active viral RNA

Total tested	1139	% Male	Age range	Median age
TTV-positive	52 (4.6%)	63	34 to 94	70
EBV-positive	251 (22%)	56	21 to 93	69
HPV-positive	68 (6.7%)	62	35 to 90	68
Positive for one or more viral RNA	330 (29%)	57		

### Co-detection RNA

TTV+EBV-positive	11 (1%)
TTV+HPV-positive	4 (0.4%)
EBV+HPV-positive	13 (1.1%)

- Machine learning distinguishes between V+ and V- patients

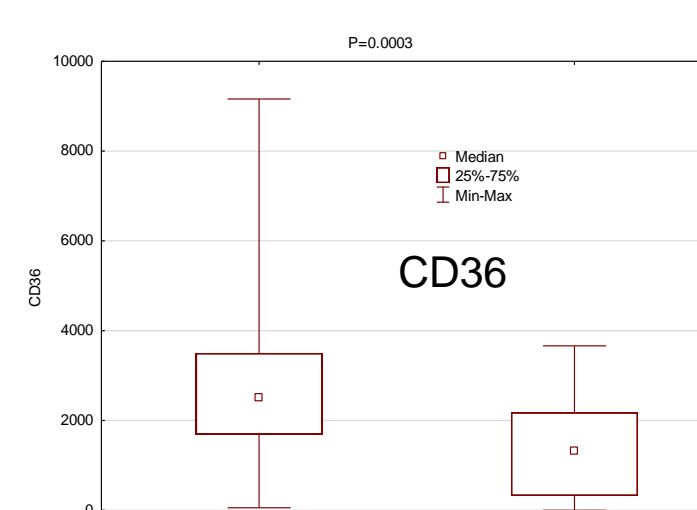
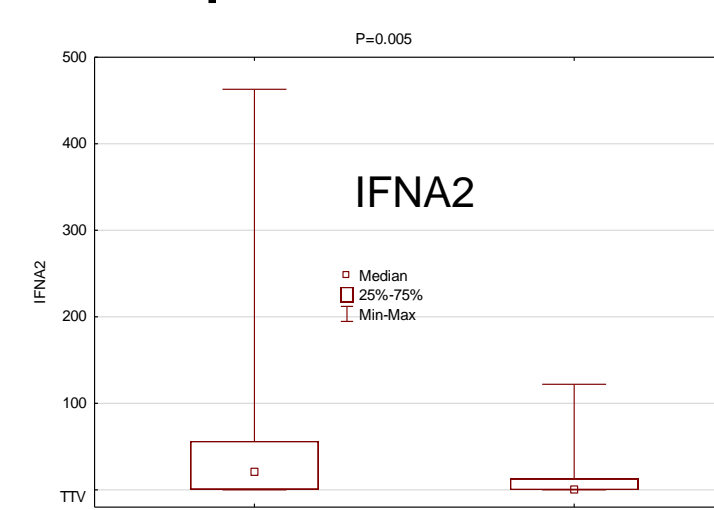
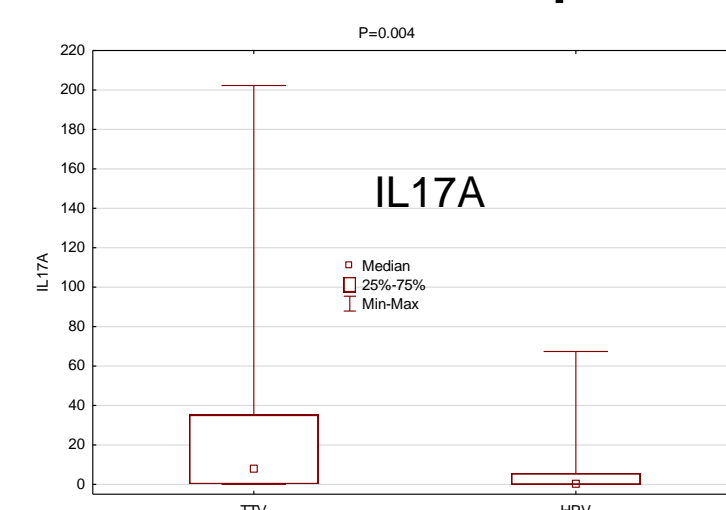


Class	Precision	Recall	F1-score
V-	0.500	0.220	0.306
V+	0.799	0.934	0.861

High B-cell markers, PD-L1, CD70 in V+

	Median expression in V+ (TPM)	Median expression in V- (TPM)	-Log10(FDR)
CD19	46.66	22.08	9
CD200	15.69	10.5	3.2
CD38	69.22	44.73	2
CD22	88.36	69.66	3.6
CD274 (PD-L1)	15.28	10.13	3.04
CD70	41.41	20.47	9
TNFRSF6B	3.4492	2.8499	7.2

- Significantly different expression of some cytokines when comparing TTV+ and HPV+ patients.
  - TTV+ patients showed significantly ↑ expression of CD36, IFNA2, and IL17A compared to HPV+ patients



## Conclusions

- Detectable active virus in plasma of patients with cancer is relatively high (29%).
- This detection is associated with a specific immune/inflammatory “activation” signature characterized by transcriptomic upregulation of PD-L1 and CD70 and increase in B-cells.
- There is no specific signature distinguishes between the V+ subgroups (TTV+ vs EBV+ vs HPV+)
- However, transcriptionally, CD36, IFNA2 and IL17A upregulation distinguished TTV+ and HPV+ cases suggesting subtle differences in immune responses depending on the virus detected.

## Future Directions for Research

Further studies are needed to correlate the presence of viral RNA with clinical outcome and susceptibility to infection. The detection of these viral RNA in circulation allows for measuring viral load and for monitoring the immune system in case of TTV and the tumor activity in cases with EBV and HPV.