Abstract #5537: HPV Status Modifies the Association Between Tissue Factor Expression and Outcomes With Tisotumab Vedotin in Cervical Cancer

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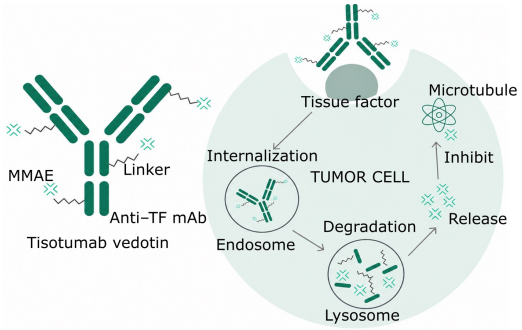
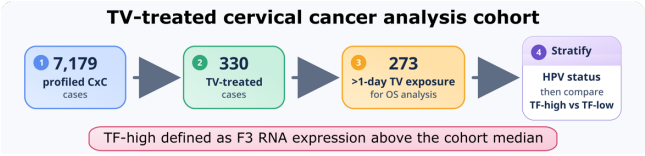
High tissue factor expression was associated with *longer overall survival* after tisotumab vedotin in *HPV-negative* cervical cancer, but this association was not observed in HPV-positive disease.

Background

- Tisotumab vedotin (TV) is a tissue factor-directed antibody-drug conjugate.
- Cervical cancer is biologically heterogeneous, with HPV-defined molecular contexts.
- Whether HPV status modifies TF-associated outcomes after TV remains unclear.



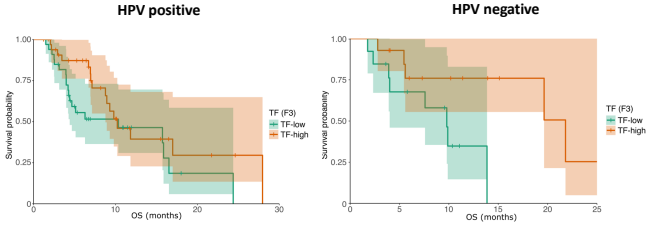
Methods



HPV-negative indicates no positive HPV16/18/31/33/45 call among available tests; incomplete HPV31/33/45 testing may affect classification.

Survival analysis

TF-high was associated with longer OS in HPV-negative disease



HR 0.60; 95% CI 0.31–1.16; P = 0.138; n = 45/34
n shown as TF-high/TF-low.

HR 0.25; 95% CI 0.07–0.98; P = 0.032; n = 14/13

TF-high vs TF-low after tisotumab vedotin: OS summary

Group	Median OS, months	HR	P value	Interpretation
Overall TV-treated	11.72 vs 9.79	0.76	0.142	Not statistically significant
HPV-positive	10.22 vs 10.35	0.60	0.138	Not statistically significant
HPV-negative	**21.81 vs 9.79**	**0.25**	**0.032**	**Longer OS with TF-high**

Median OS shown as TF-high vs TF-low. HR <1 favors TF-high.
TF-high defined by median F3 mRNA expression.
OS measured from first TV exposure to death or last contact.

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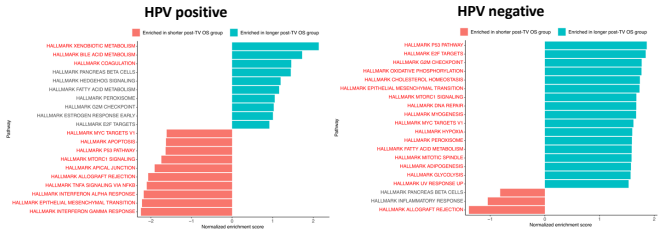
Exploratory molecular correlates

Transcriptomic correlates of post-TV OS differ by HPV status



Groups defined by above- vs at/below-median post-TV OS. Red pathway labels indicate FDR q < 0.05. WTS n for longer/shorter post-TV OS: HPV-positive 11/58; HPV-negative 6/21.

Exploratory genomic alterations associated with longer post-TV OS

- HPV-positive longer vs shorter post-TV OS: ARID1A pathogenic variants, 3/18 vs 0/41; AKT2 amplification, 2/17 vs 0/39.
- No significant genomic correlates were detected in HPV-negative comparisons.

Conclusions / Limitations

- High TF/F3 expression was associated with longer OS after TV in HPV-negative cervical cancer, but not in HPV-positive disease.
- Exploratory pathway analyses suggest HPV-stratified differences in molecular context associated with post-TV OS.
- Findings are exploratory and hypothesis-generating; the HPV-negative subgroup was small.
- Incomplete HPV31/33/45 testing may affect HPV classification.

Future directions

- Test the TF × HPV interaction in multivariable Cox models.
- Evaluate TF as a continuous biomarker and test alternative cutpoints.
- Develop integrated TV biomarker models incorporating TF, HPV status, and genomic/transcriptomic features.