**Study Design (NCT04344795)**

- TPST-1495 was dosed at 10, 25, or 50 mg BID or QD (continuous dosing) or 10 mg on Mondays and Wednesdays, or 25 mg on Mondays and Fridays (intermittent dosing) for 28 days (Figure 1). In addition, patients treated with TPST-1495 were instructed to take an aspirin at bedtime to reduce the risk of spontaneous thrombosis.

**Key Eligibility Criteria**

- Metastatic or unresectable cancer with no other approved treatments.
- Eastern Cooperative Oncology Group (ECOG) performance status of 0-1.
- Adequate bone marrow, renal, and hepatic function.
- No prior exposure to an anti-PD-1/PD-L1 or anti-CTLA-4 therapy.
- No active infection or uncontrolled intercurrent illness.
- No prior severe inflammatory bowel disease.

**Methods**

- An HIPPO3/60 method was developed and validated to determine concentrations of TPST-1495 in human serum, plasma, or plasma-derived samples.
- The peak area of the product ion of TPST-1495 was measured against the peak area of the product ion of an internal standard.

**Inhibition of PGE2-mediated tumor suppression**

- Blood samples collected at baseline and after 4 cycles of TPST-1495 were processed for the determination of levels of COX2 immunoreactivity and PGE2 immune suppressive function.

**Pharmacodynamics**

- Anti-inflammatory and immune suppressive function of TPST-1495 was measured by quantifying biomarkers associated with EP2 and EP4 blockade in patient biopsies.

**Pharmacokinetics**

- Linear PK (slope < 0.9) with C18:0, C18:1, and C18:2.

**RESULTS**

- Disease control rates of 37.5% for monotherapy and 40.9% for combination, with tumor shrinkage and prolonged stable disease (SD), including a confirmed partial response in a CRC patient.

**Conclusions & Future Directions**

- TPST-1495 is a novel inhibitor of PGE2 signaling that specifically antagonizes the tumor-promoting and immune-suppressive effects of PGE2 in a variety of cancer models.

**Acknowledgments**

- We thank the patients and their families, investigators, and coordinators for participation in the study. Ingrid Jenkins, Thomas Jenkins, PhD, provided editorial support for the poster.

**REFERENCES**

- Koo, PhD, provided editorial support for the poster.
- Jenkins, Thomas, PhD, provided editorial support for the poster.
- Tempest Therapeutics, Brisbane, CA

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**Figure 1. Prostaglandin E2 (PGE2) signaling**

- COX2-mediated production of PGE2 plays a critical role in the promotion of perturbation and immune suppression in cancer.
- TPST-1495 is a novel inhibitor of PGE2 signaling that specifically antagonizes the tumor-promoting and immune-suppressive effects of PGE2 in a variety of cancer models.

**Table 1. Percent COX2 expression in different cancer types**

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Percent COX2 Expression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oropharyngeal SCC</td>
<td>63%</td>
</tr>
<tr>
<td>Endometrial Cancer</td>
<td>63%</td>
</tr>
<tr>
<td>Anal SCC</td>
<td>63%</td>
</tr>
<tr>
<td>CRC</td>
<td>63%</td>
</tr>
<tr>
<td>Prostate</td>
<td>63%</td>
</tr>
<tr>
<td>Other</td>
<td>63%</td>
</tr>
</tbody>
</table>

**Figure 2. Leakage of alanine aminopeptidase (aAP) from primary tumors**

- Patients treated with TPST-1495 at the 25 mg dose demonstrated significant reductions in leakage of alanine aminopeptidase (aAP) from primary tumors.

**Figure 3. Tumor TNFα secretion following TPST-1495 dosing**

- The time to tumor TNFα secretion was significantly reduced in patients treated with TPST-1495 compared to placebo.

**Figure 4. Percent COX2 expression in different cancer types**

- Patients treated with TPST-1495 at the 25 mg dose demonstrated significant reductions in percent COX2 expression in different cancer types.

**Figure 5. Tumor TNFα secretion following TPST-1495 dosing**

- The time to tumor TNFα secretion was significantly reduced in patients treated with TPST-1495 compared to placebo.

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**Figure 6. Time to tumor TNFα secretion following TPST-1495 dosing**

- The time to tumor TNFα secretion was significantly reduced in patients treated with TPST-1495 compared to placebo.

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**Figure 7. Leakeage of alanine aminopeptidase (aAP) from primary tumors**

- Patients treated with TPST-1495 at the 25 mg dose demonstrated significant reductions in leakage of alanine aminopeptidase (aAP) from primary tumors.

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**Figure 8. Percent COX2 expression in different cancer types**

- Patients treated with TPST-1495 at the 25 mg dose demonstrated significant reductions in percent COX2 expression in different cancer types.

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**Figure 9. Tumor TNFα secretion following TPST-1495 dosing**

- The time to tumor TNFα secretion was significantly reduced in patients treated with TPST-1495 compared to placebo.

---

**Figure 10. Time to tumor TNFα secretion following TPST-1495 dosing**

- The time to tumor TNFα secretion was significantly reduced in patients treated with TPST-1495 compared to placebo.

---

**Figure 11. Leakeage of alanine aminopeptidase (aAP) from primary tumors**

- Patients treated with TPST-1495 at the 25 mg dose demonstrated significant reductions in leakage of alanine aminopeptidase (aAP) from primary tumors.

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**Figure 12. Percent COX2 expression in different cancer types**

- Patients treated with TPST-1495 at the 25 mg dose demonstrated significant reductions in percent COX2 expression in different cancer types.

---

**Figure 13. Tumor TNFα secretion following TPST-1495 dosing**

- The time to tumor TNFα secretion was significantly reduced in patients treated with TPST-1495 compared to placebo.

---

**Figure 14. Time to tumor TNFα secretion following TPST-1495 dosing**

- The time to tumor TNFα secretion was significantly reduced in patients treated with TPST-1495 compared to placebo.

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**Figure 15. Leakeage of alanine aminopeptidase (aAP) from primary tumors**

- Patients treated with TPST-1495 at the 25 mg dose demonstrated significant reductions in leakage of alanine aminopeptidase (aAP) from primary tumors.

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**Figure 16. Percent COX2 expression in different cancer types**

- Patients treated with TPST-1495 at the 25 mg dose demonstrated significant reductions in percent COX2 expression in different cancer types.

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**Figure 17. Tumor TNFα secretion following TPST-1495 dosing**

- The time to tumor TNFα secretion was significantly reduced in patients treated with TPST-1495 compared to placebo.

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**Figure 18. Time to tumor TNFα secretion following TPST-1495 dosing**

- The time to tumor TNFα secretion was significantly reduced in patients treated with TPST-1495 compared to placebo.

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**Figure 19. Leakeage of alanine aminopeptidase (aAP) from primary tumors**

- Patients treated with TPST-1495 at the 25 mg dose demonstrated significant reductions in leakage of alanine aminopeptidase (aAP) from primary tumors.

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**Figure 20. Percent COX2 expression in different cancer types**

- Patients treated with TPST-1495 at the 25 mg dose demonstrated significant reductions in percent COX2 expression in different cancer types.

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**Figure 21. Tumor TNFα secretion following TPST-1495 dosing**

- The time to tumor TNFα secretion was significantly reduced in patients treated with TPST-1495 compared to placebo.

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**Figure 22. Time to tumor TNFα secretion following TPST-1495 dosing**

- The time to tumor TNFα secretion was significantly reduced in patients treated with TPST-1495 compared to placebo.