Abstract ID: AB 010

A Phase 1 trial of PRTH-101, a monoclonal antibody targeting discoidin domain receptor 1 (DDR1), alone or in combination with pembrolizumab, for the treatment of thymic malignancies

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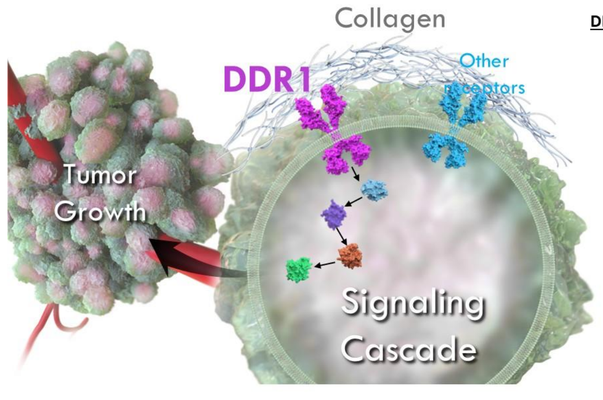
BACKGROUND

There are no FDA-approved therapies for recurrent/metastatic thymic epithelial cancers (TEC) and current treatments with chemotherapy and immunotherapy leave considerable room for improvement. DDR1 is a collagen receptor expressed on tumor epithelial cells. DDR1 binding to collagen surrounding tumor cells results in highly aligned collagen fibers, and exclusion of CD8+ T cells from the tumor (i.e., immune exclusion), precluding an effective anti-tumor response. High DDR1 expression has been observed in TECs and other epithelial tumor types. Furthermore, published data suggest that high DDR1 expression is associated with poor prognoses and lack of response to immunotherapies.

PRTH-101 is a humanized monoclonal antibody that blocks the interaction of collagen with the extracellular domain of DDR1; it is being tested in a Phase 1 clinical trial (PRTH-101-0001) as a single agent (Phase 1a), in combination with pembrolizumab (Phase 1b) and alone or in combination with pembrolizumab in tumor-specific expansion cohorts (Phase 1c), including thymic epithelial carcinoma. PRTH-101 doses up to 1600 mg have shown no dose-limiting toxicities alone or together with pembrolizumab. Clinical, pharmacokinetic, and target engagement data from 68 patients have informed a recommended Phase 2 dose of 1200 mg, which is being tested in Phase 1c, with or without pembrolizumab.

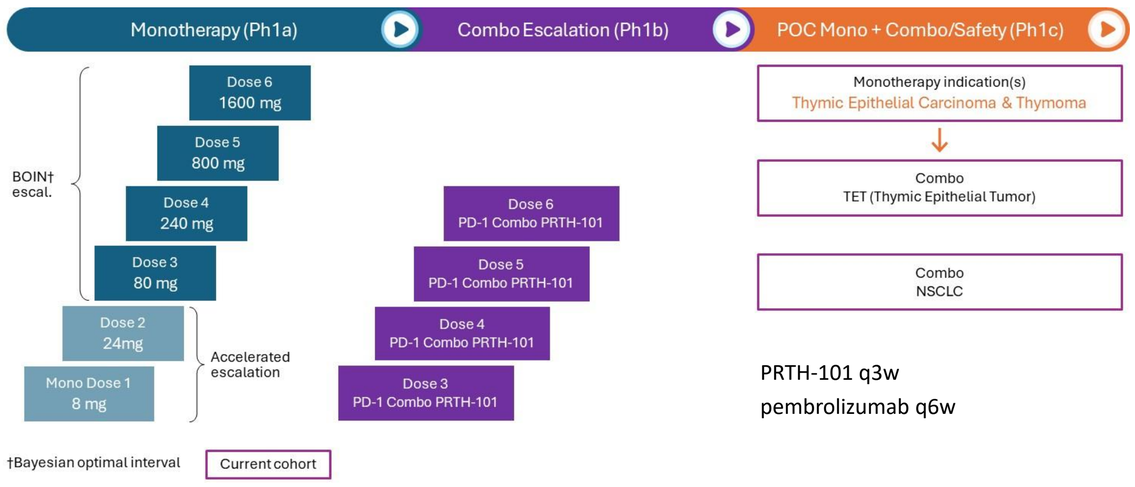


DDR1 role in cancer

- DDR1 is over-expressed in many cancers and fibrosis, and associated with poor survival
- Tumor DDR1 activity is associated with collagen alignment and immune exclusion
- Collagen binding leads to DDR1 receptor clustering, induction of pDDR1, and signaling
- Highly structured collagens are prognostic and predictive in Cancer (Ray *et al.*, Curr. Opin. Cell Biol., 2021; Chen *et al.*, JAMA Netw Open, 2021)
- DDR1 is associated with resistance to PD-L1 inhibitor therapy (Necchi *et al.*, Ann. Onc. 2017; You *et al.*, J. Natl. Cancer Inst. 2022)
- Currently no DDR1 kinase inhibitors in clinical development

METHODS and RESULTS

PRTH-101-0001 Clinical Trial Design



Study Summary (as of 12 September 2025)

Eligibility

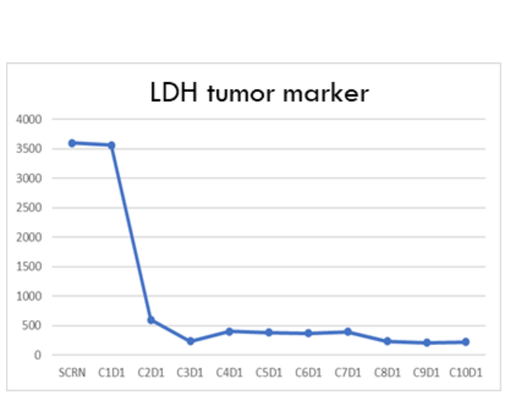
- Metastatic or unresectable measurable solid malignancy for which no established therapy is of benefit, or has been declined by the patient
- ECOG performance status 0 – 1; no significant co-morbid illness
- Prior PD-1/PD-L1 therapy permissible; no prior ICI Adverse Events AE ≥ Grade 3 or Grade 2> myocarditis or pneumonitis
- Immune-mediated AEs must have resolved to Grade 1, except vitiligo, well-controlled endocrinopathies, or Grade 2 peripheral neuropathy.
- No uncontrolled CNS disease, hepatocellular cancer, sarcoma, or GBM

Status

- 69 subjects enrolled (enrollment complete for Phase 1a and Phase 1b); 1 ongoing in Phase 1 b and 8 ongoing in Phase 1c
- Median age: 63 (range 25-83); Sex: F = 28, M = 40
- Prior therapies: median = 4 (range 0 – 8); prior immunotherapy = 33
- Tumor diagnoses:
  - Thymic carcinoma = 20; thymoma = 3; CRC = 14; lung = 6; PDAC = 5; ovarian = 5; SCCNH = 2; other = 13
- Time on treatment: median = 8 weeks (range <3 to 67)
- Well tolerated; no dose-limiting toxicities
- Phase 1c does determined (1200 mg, q3w); dosing thymic cohort
- Projected completion of thymic cohort enrollment: Q2 2026

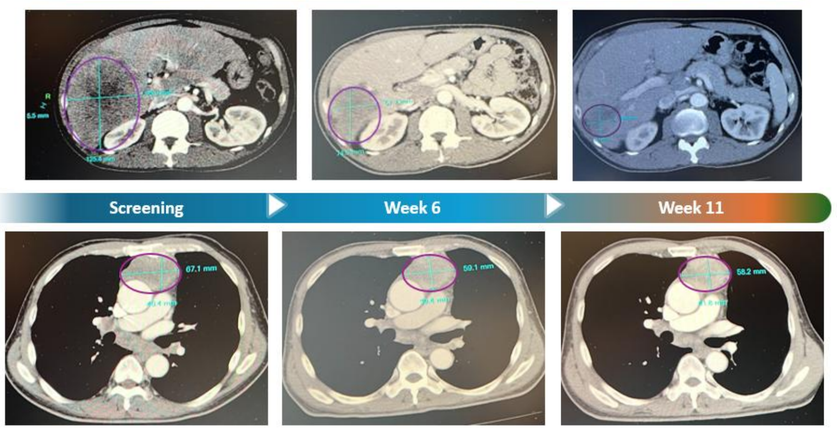
Partial Response in thymic epithelial carcinoma: 62-YO male, avid runner, cough and chest tightness, no prior Rx, PD-L1 negative

- Explosive tumor growth in 3 months from diagnosis
- 1200 mg PRTH-101 + pembrolizumab
- Has been on study for 8 months
- Normalization of LDH levels
- Publications show that PD-L1-negative thymic cancers do not respond to single-agent pembrolizumab (Giaconne *et al.*, 2017; Cho *et al.*, 2018)



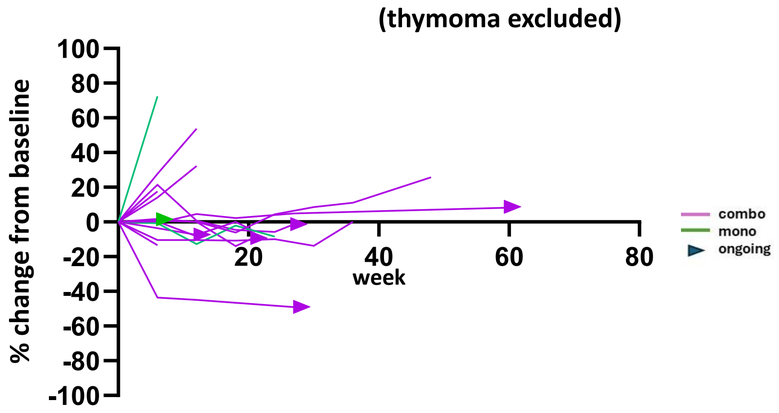
Suggests benefit of combination treatment with PRTH-101

Liver Mass #1



Primary Tumor

Changes from Baseline in Thymic Tumors Treated with PRTH-101 (thymoma excluded)

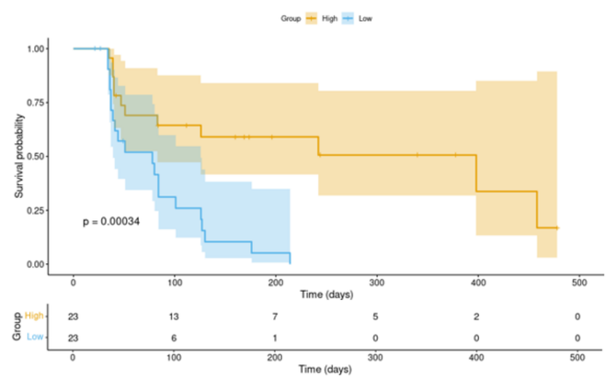


PRTH-101-0001 Trial

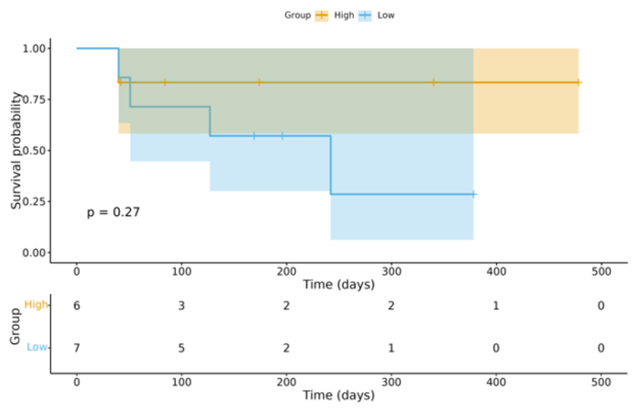
- **Median PFS (ongoing) for TEC patients:**
  - **5.7 months (safety dataset)**
  - **7.1 months (event extraction dataset)**

Giaccone trial PFS = 4.2 months
(Giaccone *et al.*, Pembrolizumab in patients with thymic carcinoma: a single-arm, single-centre, phase 2 study, Lancet Oncol., 2018)

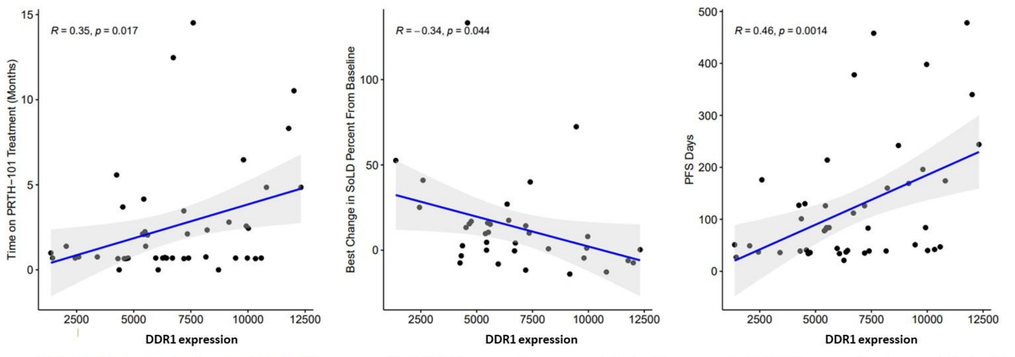
DDR1 expression correlates with PFS (n = 46), all tumors



DDR1 expression trends with PFS in thymic tumors



DDR1 expression is associated with response to PRTH-101 treatment



High DDR1 expression is correlated with longer times on treatment

High DDR1 expression is correlated with decreases in sum of lesion diameters

High DDR1 expression is correlated with longer progression-free survival

CONCLUSIONS

- **Phase 1 testing of PRTH-101 has shown evidence of clinical benefit in patients with thymic epithelial cancers.**
- **A Partial Response (PR) has been observed in a patient with a rapidly growing tumor and metastases.**
- **Median PFS (ongoing) for TEC patients is 5.7 months (safety dataset) and 7.1 months (event extraction dataset).**
- **Tumor response to PRTH-101 is correlated with the expression of DDR1, the target of PRTH-101.**
- **DDR1 and PD-L1 expression data, combined with PFS data, suggest that PRTH-101 contributes to or is responsible for observed PFS in these patients.**
- **PRTH-101 testing has shown no nonclinical toxicities or dose-limiting clinical toxicities in initial Phase 1 testing at any dose level.**
- **A PR has also been observed in a NSCLC patient, and a prolonged SD was observed in another NSCLC patient, suggesting that PRTH-101 also shows promise for the treatment of NSCLC.**
- **Based on these data, a Phase 2 trial in patients with advanced thymic malignancies is planned (please see AB 16).**

The Sponsor and Investigators are grateful to the patients who have participated in this trial, and to their families.

Drs. Eder, Schürpf, Mueller, and Macdonald and Ms. Webster are employees of Incendia Therapeutics. Dr. Clifton is a former employee of Incendia Therapeutics. The remaining authors are Investigators in the PRTH-101-0001 trial.

INCENDIA THERAPEUTICS