**TPS11580** **Poster Session**

# An open-label phase 1/2 study of DCC-3009 monotherapy in patients with advanced gastrointestinal stromal tumor.

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**Background:** Gastrointestinal stromal tumor (GIST) is the most common sarcoma of the gastrointestinal tract. *KIT* and platelet-derived growth factor receptor $\alpha$ (*PDGFRA*) mutations remain the key oncogenic drivers in the majority of patients with advanced GIST, with acquired secondary drug-resistant mutations contributing to the heterogeneity and complexity of the disease. The diversity of these resistance mutations allows escape from standard-of-care tyrosine kinase inhibitor (TKI) therapy, creating an unmet need for novel therapies that inhibit all clinically relevant GIST-driving mutations. DCC-3009 is an investigational, highly potent, and selective switch-control KIT and PDGFRA inhibitor designed to act against known clinically relevant primary and secondary GIST-driving mutations while limiting off-target effects. Preclinical data showed that DCC-3009 has strong antitumor effects in xenograft models driven by resistant *KIT* mutations, optimized solubility and oral bioavailability, and low risk of cytochrome P450 inhibition. Here, we describe an ongoing phase 1/2 study evaluating DCC-3009 as a monotherapy in patients with advanced GIST. **Methods:** This study is a multicohort, open-label, phase 1/2 trial evaluating the safety, tolerability, and efficacy of DCC-3009 in patients with advanced GIST (NCT06630234). This trial uses a modular approach, with each module defined according to the therapy (DCC-3009 alone or in combination with other anticancer agents) and divided into 2 parts (dose escalation and dose expansion). For inclusion in the DCC-3009 monotherapy dose escalation, adult patients ($\geq$18 years) must have histologically or cytologically confirmed advanced GIST with documented *KIT* or *PDGFRA* mutation and progression on or intolerance to at least 1 approved TKI regimen in the advanced setting (imatinib if *KIT*-mutant). Patients must have at least 1 measurable lesion per modified Response Evaluation Criteria in Solid Tumors version 1.1 (mRECIST v1.1) and an Eastern Cooperative Oncology Group Performance Status of 0 or 1 at screening. Exclusion criteria include receiving systemic anticancer therapy (encompassing investigational agents) within 14 days or less than 5 half-lives, radiotherapy within 14 days prior to first dose of study drug, prior or concurrent malignancy requiring treatment or expected to need treatment for active cancer, known allergy or hypersensitivity to the study drug components or any of its excipients, and impaired oral absorption or malabsorption syndrome. Enrolled patients across monotherapy dose escalation will receive DCC-3009 orally in 28-day cycles. The primary outcome measures for monotherapy dose escalation include safety assessment. Secondary outcome measures include objective response rate, duration of response, and progression-free survival by mRECIST v1.1, as well as overall survival and pharmacokinetics. Clinical trial information: NCT06630234. Research Sponsor: Deciphera Pharmaceuticals, LLC.