

## **DEKA-1 a Dose-Finding Phase 1 Trial: Observing Safety and Biomarkers using DK210 (EGFR) for Inoperable Locally Advanced and/or Metastatic EGFR+ Tumors with Progressive Disease Failing Systemic Therapy**

**Authors :** Spira A., Marabelle A., Kientop D., Moser E., Mumm J.

**Abstract :** Background: Both interleukin-2 (IL-2) and interleukin-10 (IL-10) have been extensively studied for their stimulatory function on T cells and their potential to obtain sustainable tumor control in RCC, melanoma, lung, and pancreatic cancer as monotherapy, as well as combination with PD-1 blockers, radiation, and chemotherapy. While approved, IL-2 retains significant toxicity, preventing its widespread use. The significant efforts undertaken to uncouple IL-2 toxicity from its anti-tumor function have been unsuccessful, and early phase clinical safety observed with PEGylated IL-10 was not met in a blinded Phase 3 trial. Deka Biosciences has engineered a novel molecule coupling wild-type IL-2 to a high affinity variant of Epstein Barr Viral (EBV) IL-10 via a scaffold (scFv) that binds to epidermal growth factor receptors (EGFR). This patented molecule, termed DK210 (EGFR), is retained at high levels within the tumor microenvironment for days after dosing. In addition to overlapping and non-redundant anti-tumor function, IL-10 reduces IL-2 mediated cytokine release syndrome risks and inhibits IL-2 mediated T regulatory cell proliferation. Methods: DK210 (EGFR) is being evaluated in an open-label, dose-escalation (Phase 1) study with 5 (0.025-0.3 mg/kg) monotherapy dose levels and (expansion cohorts) in combination with PD-1 blockers, or radiation or chemotherapy in patients with advanced solid tumors overexpressing EGFR. Key eligibility criteria include 1) confirmed progressive disease on at least one line of systemic treatment, 2) EGFR overexpression or amplification documented in histology reports, 3) at least a 4 week or 5 half-lives window since last treatment, and 4) excluding subjects with long QT syndrome, multiple myeloma, multiple sclerosis, myasthenia gravis or uncontrolled infectious, psychiatric, neurologic, or cancer disease. Plasma and tissue samples will be investigated for pharmacodynamic and predictive biomarkers and genetic signatures associated with IFN-gamma secretion, aiming to select subjects for treatment in Phase 2. Conclusion: Through successful coupling of wild-type IL-2 with a high affinity IL-10 and targeting directly to the tumor microenvironment, DK210 (EGFR) has the potential to harness IL-2 and IL-10's known anti-cancer promise while reducing immunogenicity and toxicity risks enabling safe concomitant cytokine treatment with other anti-cancer modalities.

**Keywords :** cytokine, EGFR over expression, interleukine-2, interleukine-10, clinical trial

**Conference Title :** ICCIB 2023 : International Conference on Cancer Immunotherapy and Biomarkers

**Conference Location :** Paris, France

**Conference Dates :** April 13-14, 2023