

## **Active-specific anti-cancer immunotherapy with a poly-peptide containing multiple cytotoxic-T-lymphocyte epitopes of Thymidylate synthase**

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TSPP is a 27-mer poly-peptide containing three known CTL epitopes with HLA-A2.1 binding motifs of the thymidylate synthase (TS), an enzyme over-expressed in cancer cells and critical for their replication. We have tested the safety and the biological activity of TSPP vaccination in advanced cancer patients in a phase Ib trial.

Twenty-one pre-treated/metastatic cancer patients with a good *performance status* (ECOG < 2), and no severe organ failure or immunological disease were enrolled in the study and administered with TSPP alone (arm-A) or in combination with GM-CSF and IL-2 (Arm B) in order to identify the maximal-tolerated-dose (MTD) and the most effective-biological-dose (MEBD) of the vaccine.

There was no grade 4 toxicity. The most common adverse events were grade 2-3 local dermatological reaction in the vaccine injection site, cough, rhinitis, fever, poly-arthralgia, gastro-enteric symptoms and to a lesser extent, hypertension and hypothyroidism. We detected a TS-specific CTL response, modulation in inflammatory markers and a general increase in auto-antibodies like ANA, ENA, cANCA and pANCA. MTD of TSPP vaccine was not achieved, while MEBD resulted in a range of 200-300 µg. We also recorded a partial response and six stabilizations of disease (SD) in the patients of arm A, and two SD those of arm B. Our results offer the rationale to evaluate the anti-tumor activity of TSPP alone in further trials.