AST-008: A Novel Approach to TLR9 Agonism with PD-1 Blockade for Anti-PD-1 Refractory Merkel Cell Carcinoma (MCC) and Cutaneous Squamous Cell Carcinoma (CSCC)

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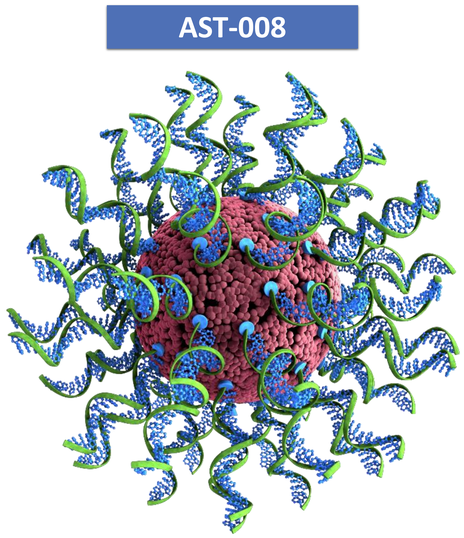
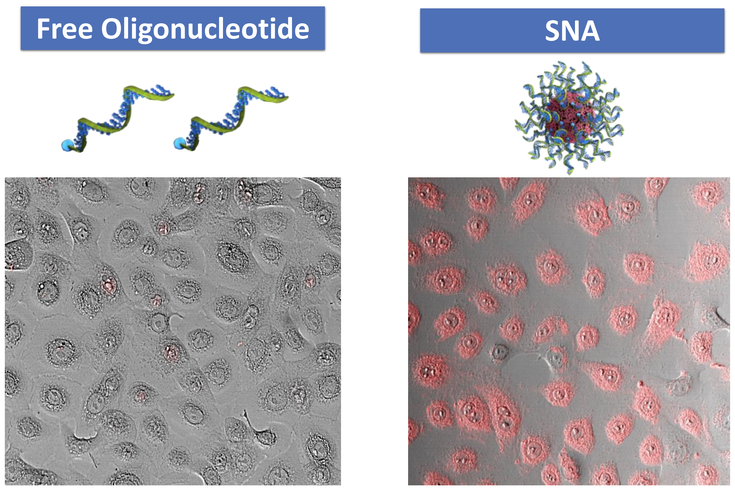
Background

AST-008 is a toll-like receptor 9 (TLR9) agonist in a spherical nucleic acid (SNA) format with potent immune-stimulatory properties



SNAs are dense, radial arrangements of nucleic acids that have increased cellular uptake (below) and an optimal presentation of the oligonucleotides for TLR9 agonism vs free oligonucleotides



Key Study Design Elements

Open label, multicenter phase 1b/2 dose escalation/expansion design study in progress (NCT03684785)

Phase 2s: Intratumoral (IT) AST-008 plus pembrolizumab or cemiplimab for PD-(L)1 resistant MCC and PD-1 resistant CSCC, respectively. Phase 1b enrolled all solid tumors.

Key study design features: Safety

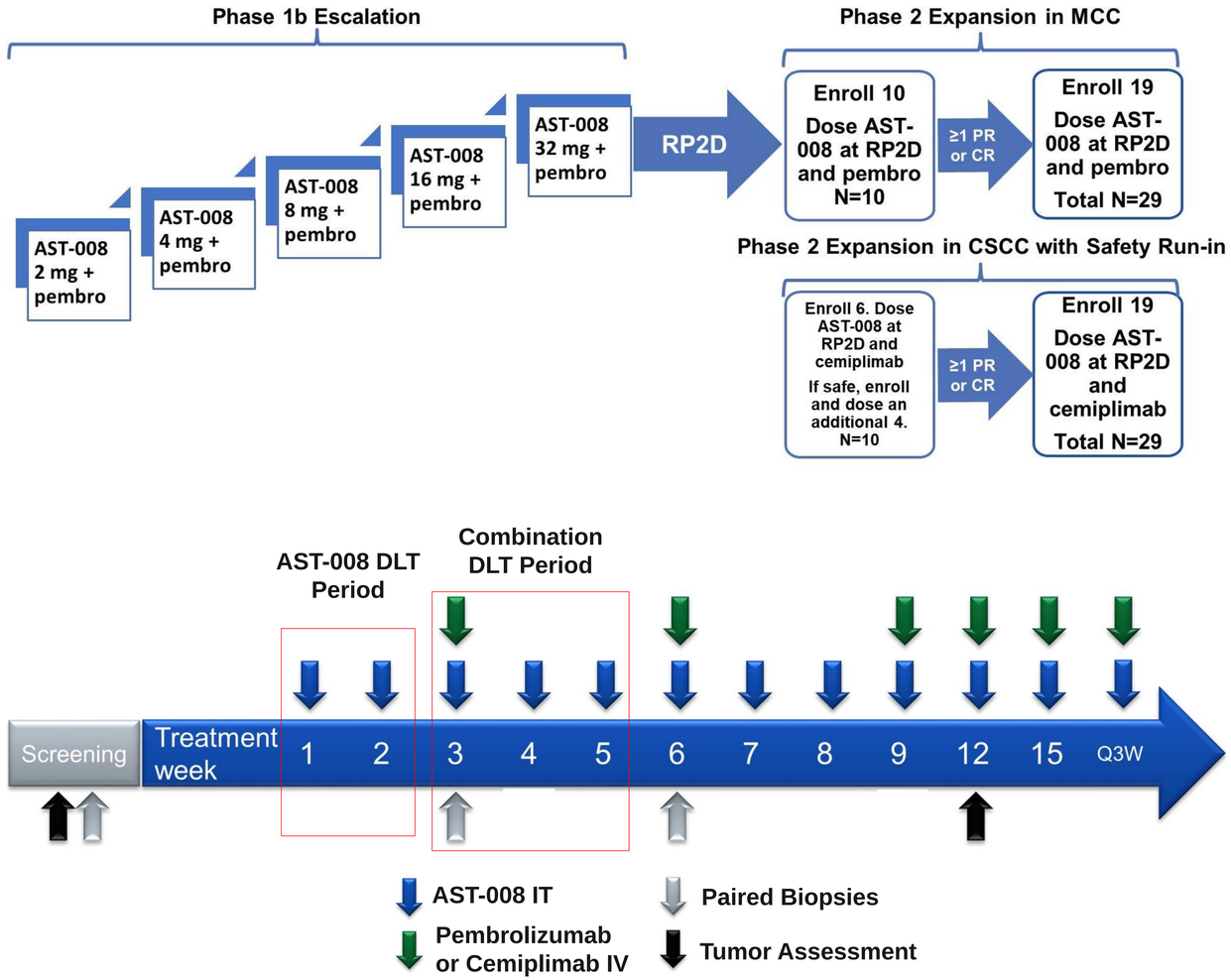
- Dose escalation used a double dose limiting toxicity period (DLT) design. AST-008 dosed IT alone for 2 weeks, then the anti-PD-1 antibody is added. Efficient differential assessment of safety and tolerability of AST-008 and the combination
- FDA allowed dose expansion cohort of AST-008 plus cemiplimab in CSCC after performing dose escalation with AST-008 plus pembrolizumab

Key study design features: Efficacy

- 2 or more RECIST 1.1-evaluable lesions required for enrollment. One lesion is to remain uninjected with AST-008 over the course of the study to observe abscopal effects

Key study design features: Pharmacodynamics

- Paired serial biopsies taken at baseline, after AST-008, and after combination. One lesion is injected with AST-008 over the course of the study, one is not (termed target and witness lesions). Enables differential assessment of local and distant effects of AST-008 and the combination



AST-008, Anti-PD-1 Antibodies, and the Cancer Immunity Cycle

AST-008 and anti-PD-1 pharmacodynamics are expected to synergize and propagate steps of the cancer immunity cycle (*Cancer Res* **2019**;79(13 Suppl):abstract CT044)

This study is currently recruiting into Phase 2. Email edegoma@exicuretx.com if you are interested in participating as an investigator

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