Background and Purpose

- **Mechanism of Action**
  - CD8+ T cells require a 21-day antigen receptor (TCR) and a T-cell-specific cytokine stimulation for engagement and activation in the tumor
  - Tumor antigen recognition by CD8+ cells (TCR) elicits the IL-10 and IL-20 cytokine release
  - IL-10 suppresses CD8+ T-cell function and PD-1 expression
  - PD-1 binds the TCR signal in CD8+ T cells and induces negative feedback ("immune checkpoint")

**FIGURE 8-10**: IL-10 (AM0010) induces the activation and survival of CD4 T cells through phosphorylation of the transcription factors STAT4 and STAT6. Regulation of IL-10 ensures the activation of the T-cell receptor (TCR) in CD8+ T cells, leading to IL-10-mediated PD-1 expression.

**Mechanism of Action**

**AM0010 Monotherapy Dose Escalation**

1. Patients (56) treated at 20 µg/kg dose had complete response (CR) at 2 months
2. Patients (56) treated at 40 µg/kg dose had objective response
3. Patients (56) continued treatment at 100 µg/kg (censored cohort 100, 50% and 40%)

**AM0010 Dose Escalation - Clinical Activity**

**AM0010 Dose Escalation - Melanoma and RCC**

- 4 patients (16) evaluable patients had partial response (PR)
- 12 (16) evaluable patients had stable disease
- Several patients discontinued due to early disease control

**AM0010 Monotherapy (20g/kg) (n=16)**

- 6 (40%) of 16 evaluable patients had partial response
- 12 (75%) of 16 evaluable patients had stable disease
- Several patients discontinued due to early disease control

**AM0010 mediated expansion of the adaptive CD8+ T cell repertoire**

**Mechanism Based Combination with AM0010**

**Conclusion and Outlook**

- **Peptide-Mediated Methods - Preclinical and Prognostic Results**
  - 29 patients with immune sensitive tumor types (Melanoma, RCC) (60%) were treated with pegylated IL-10 (40/250 or 2/10 g/kg) and pembrolizumab

- The combination was well tolerated at 10 and 20µg/kg AM0010 – no additional toxicities were observed

- RCC (n=6): OS, DCR 100% at 16 weeks, NCR (n=18): OS, DCR 80% at 16 weeks