Varilumab (CD27) is a human monoclonal antibody to CD27 that is being studied for its ability to activate and maintain T cell receptor occupancy for up to 180 days after administration, allowing for a single administration every 28 days. The combination with other immunotherapies such as checkpoint inhibitors is being evaluated, and the phase 2 studies in renal cell carcinoma and colorectal cancer have shown promising results. The study presented at ASCO 2023 demonstrated a significant increase in response to melanoma antigens in melanoma patients treated with varilumab. The phase 3 trials in renal cell carcinoma and colorectal cancer are ongoing.

**Clinical Activity**
- **Epitope specificity:** Tumor-infiltrating lymphocytes were generated and expanded with epitope-specific peptide. After restimulation, the lymphocytes were compared with the peptide used for restimulation.
- **Dose escalation:** Three dose levels were evaluated: 1 mg/kg, 2 mg/kg, and 3 mg/kg.
- **Safety profile:** The treatment was generally safe and well tolerated. The most common adverse events included asthenia, headache, and diarrhea.
- **Efficacy:** The response rate was higher in patients treated with varilumab compared to those treated with saline.

**Conclusion**
- Varilumab demonstrates clinical activity and safety in heavily pretreated renal cell carcinoma patients, with a tolerable safety profile and promising response rates. Further studies are needed to confirm these findings and explore the potential of combination therapies with checkpoint inhibitors.

**Future Directions**
- Future studies will aim to evaluate the combination of varilumab with checkpoint inhibitors and other immunotherapies in renal cell carcinoma and colorectal cancer.
- The role of varilumab in patients with uveal melanoma who previously failed ipilimumab will be explored.

**Support for Combination Studies of Varilumab**
- Varilumab has shown promise in combination with other immunotherapies, particularly checkpoint inhibitors, in the treatment of renal cell carcinoma and colorectal cancer.