Combination of monalizumab and durvalumab as a potent immunotherapy treatment for human solid cancers

Caroline Soulas1, Romain Remark1, Julie Lopez1, Elodie Bonnet1, Flavien Caragueul1, Ana Lalanne2, Caroline Hoffmann2, Caroline Denis1, Thomas Arnoux1, Clarisse Caillé1, Fabien Chauvin1, Arnaud Dujardin1, Guillaume Habib1, Olivier Lantz1, Cécile Bonnafous1, Eric Vivier1, Pascale André2
1- Innate Pharma, Marseille, France; 2- Institut Curie, Paris, France; 3- Centre d’Immunologie de Marseille Luminy, Marseille, France.

Background

Monalizumab (IPH2201) is a first-in-class humanized IgG2A, which is expressed as a heterodimer with CD94 on subsets of NK cells, CD8+ and tumor-infiltrating CD8+ T cells. This inhibitory receptor binds to HLA-E (Human Leucocyte Antigen-E), in humans and to Qa-1 α in mice. HLA-E is upregulated on cancer cells of several solid tumors, providing a negative regulatory signal to tumor-infiltrating lymphocytes (TIL). Monalizumab blocks binding of CD94:monalizumab to HLA-E, reducing inhibitory signaling and thereby enhancing NK and T cell responses. PC/IPD-1L inhibitors are successfully being used to treat patients with a wide variety of cancers. Combined blockade of NKG2A:IPD-2 and PD-1/PD-1L may be a promising strategy to further fight cancer by activating both the adaptive and innate immune pathways.

Here, we describe NK and CD8+ T cells infiltrates in several human solid tumors by immunostaincostaining (HC) and multicolor flow cytometry. We then studied the effects of cell therapy targeting both pathway on primary human NK and CD8+ T cells and the efficacy of this combination in a syngeneic mouse model.

NK2GA and PD-1 are expressed on tumor infiltrating NK and CD8+ T cells from cancer patients

A Lung cancer patients

B Head and Neck cancer patients

CD8+ T, NK and NKG2A+ immune cells are present in several solid cancer types that express HLA-E

Higher HLA-E expression is observed on solid tumors compared to PD-L1

Conclusions

• Tumor infiltrating NK and CD8+ T cells expressing NKG2A and PD-1 are present in several cancer types.
• HLA-E is expressed by tumor cells in the large majority of solid tumors compared to PD-L1.
• Blocking both NKG2A/HLA-E and PD-1/PD-1L pathways could enhance responses of NK and CD8+ T cells that are present in close contact to tumor cells and further boost innate and adaptive immunity.
• Together, these data support the rationale for ongoing clinical trials investigating the monalizumab/durvalumab combination (NCT02871435).