Immune checkpoint blockade plus interferon-γ add-on antifungal therapy in the treatment of refractory Covid-associated pulmonary aspergillosis and cerebral mucormycosis

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Mucormycosis and aspergillosis are life-threatening fungal infections (IFI).

Rescue therapies are needed for patients not responding to conventional treatment. Recently published studies in animal models and human case reports suggest a potential benefit of checkpoint inhibitors.

Positive Rhizopus & Mucor PCR in serum
Negative Rhizopus & Mucor PCR in serum

Figure 1. Timeline

Figure 2. Evolution of MRI and serum Mucorales PCR under treatment

Figure 3. Evolution of serum galactomann under treatment

Figure 4. Evolution of the percentage of CD4 and CD8 T cells expressing PD-1 and HLA-DR under immunotherapy

At MROC diagnosis
After 10 days of anti-fungal therapy with L-Amb
After 2 weeks of adjuvant immunotherapy
One month after the stop of adjuvant immunotherapy

Nivolumab

100% 50% 0%
PD1 expression

0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 weeks

0 before treatment
After 2 weeks of antiPD-L1/IFNγ
After 3 weeks of antiPD-L1/IFNγ

100% 50% 0%
HLA DR expression

0 before treatment
After 2 weeks of antiPD-L1/IFNγ
After 3 weeks of antiPD-L1/IFNγ

• Although the patient did not survive, the initial clinical response obtained with anti-PD-1 plus IFN-γ add-on dual antifungal therapy and surgical management is encouraging.

• Combination immunotherapy might be considered as salvage treatment of life-threatening IFI unresponsive to conventional therapy. Further studies will be needed to determine its optimal timing and role in the current therapeutic arsenal.

• As patients with IFI are usually particularly fragile and under a lot of concomitant medications, the use of immune checkpoint inhibitor must be carefully monitored (risk of severe, notably autoimmune, adverse effects).